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SUPPLEMENT 270

Frontal Sinus Surgery

BY

ROGER HAYS LEHMAN

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ROGER HAYS LEHMAN

Presented as Candidate's thesis to the American Laryngological, Rhinological and Otological Society October 1969

Veterans Administration Center and Marquette University School of Medicine, Milwaukee, Wisconsin, USA

I Introduction

Frontal sinus surgery comprises only a small part of the current otolaryngologic practice. The classical clinical pictures of acute and chronic suppuration have been modified by the antibiotic and chemotherapeutic agents. Lack of symptoms and absence of signs have made specific diagnoses more difficult. Latent infections do exist, and the probability of intracranial complications arising from them is still very real.

Early surgical procedures were radical and designed to prevent intracranial complications. The functional and cosmetic results left much to be desired. An era of conservatism in surgery followed the advent of the antibacterial drugs. Upon recognition of increasing numbers of patients with residual disease and complications, reports of more extensive surgery began to appear. There has been a recent revival and modification of older techniques with improved results.

A current review of frontal sinus surgery performed over a period of two decades seems appropriate at this time. Consideration will be given to the historical background, surgical anatomy, physiologic principles, and operative procedures.

II History

In 1870 Wells (1) reported a patient with a pyocele involving the fronto-ethmoid cell complex who was cured by an external and internal nasal drainage procedure.

Ogston ( ) in 1884 advocated trephining of the frontal sinuses for catarrhal diseases unresponsive to medical therapy. He used a midline vertical incision, elevated the periosteum, entered the sinus with a sixpenny size trephine crown and enlarged the opening with chisel. Diseased mucous membrane was removed, and a drainage tube was placed into the nose. Three patients described were asymptomatic for a considerable period of time.

Obliteration of the frontal sinus performed by Kuhnt (3) in 1895 included removal of the anterior wall, paring 0.5 cm above the orbital margin. He cited Runge as performing a similar operation 150 years earlier and quoted techniques of his contemporaries, Hebinger & Jansen, who recommended intranasal drainage. Kuhnt, however, favored external drainage alone and daily postoperative irrigations of the cavity with sublimate.

Röpke (4) in 1898 modified the procedure by removing the anterior, inferior and medial walls of the frontal sinus to expose adequately involved ethmoid cells. Riedel (5) stressed the importance of taking the inferior sinus wall.

The osteoplastic anterior wall approach to the frontal sinus was described by Schönborn (6) in 1894. Brieger (7), in 1895 reported upon the use of a skin-periosteum-bone flap which was successfully removed and reimplanted. In 1904 Winckler (8) suggested an osteoplastic procedure with the flap hinged above the orbital margin. He used this approach only when no bone or soft tissue was involved by disease and when no intracranial complications were suspected. Beck (9) and

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Hoffman (10) later made further minor alterations of the osteoplasty

After the turn of the century Killian (11) proposed a frontal sinus operation which included removal of the anterior and inferior walls except for a bridge of bone in the supraorbital area Later he included the frontal process of the maxilla in his dissection to facilitate ethmoid cell exposure and establish a wide opening into the nose Ethmoid cells were exenterated and a flap of nasal mucosa was formed to maintain an open communication with the denuded frontal sinus. Lothrop (12) suggested circumventing the nasofrontal duct on the diseased side by removal of the intersinus septum and utilization of the opposite nasofrontal duct for drainage

The operation originally proposed by Jansen (13) in 1902 and later modified by Lynch (14) in 1921 was considered the procedure of choice for the next several decades This procedure consisted of removal of the frontal sinus floor preservation of the anterior wall and exenteration of the adjoining ethmosphenoid cell system Lynch advocated the removal of every vestige of frontal sinus mucosa, and the concurrent treatment of any intranasal obstruction or antral disease Ritter (15) modified the Jansen technique by elevating the anterior sinus wall laterally as a flap

These extensive surgical procedures often did not eliminate disease and the search continued for better therapy for frontal sinusitis Skillern (16) advocated a conservative approach to sinus surgery at this time Smith (17) used a Thiersch skin graft around a rubber tube to maintain the patency of the nasofrontal duct and reported occlusion in only 3 of 100 patients Sewall (18) McNaught (19) Boyden (20) and Ogura (21) published reports upon methods of reconstruction of the nasofrontal duct with adjoining mucoperiosteal flaps, as Killian (11) had originally suggested.

The use of prosthetic devices to maintain the patency of the nasofrontal duct also had proponents Ingals (22) originally had devised a gold tube, and Goodale (23) suggested tantalum but Hugenberg & Williams (24) reported a foreign body reaction to it. Erich & New (25) used an acrylic obturator with success

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Subsequently in view of the continued high rate of recurrent disease with previous procedures Gibson & Walker (27) MacBeth (28), Tato Sibbald & Bergaglio (29) Bergara & Itoiz (30) and Goodale & Montgomery (31) utilized the osteoplastic flap approach and reported favorable results Then in 1964 Goodale & Montgomery (32, 33) combined the osteoplastic flap and the obliteration of the sinus with a fat graft Sanders (34) stressed the importance of a thorough removal of sinus mucosa accomplished through the floor of the frontal sinus rather than by the osteoplastic flap

In 1967 Kirchner Toledo & Robison (35) described a modification of the osteoplastic flap to facilitate removal of lesions of the orbit as well as the frontal sinus and frontal bone Failla (36) recently recommended suture of the mucosa at the nasofrontal duct level in ablations following frontal sinus fracture

III Surgical Anatomy

The frontal sinus (37) is an outgrowth of the frontal recess in the cephalo-ventral end of the middle turbinate where frontal furrows or pits evaginate to form the frontal cells. It begins to invade the frontal bone in the second year of life but complete development is not reached until about the sixteenth year Consequently it does not have clinical significance until approximately this time

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tion of the size of the sinuses. They are rarely symmetrical and vary in depth and shape as well. Each cavity is partially divided by horizontal and vertical septa. The capacity varies from 1 to 44 cm and the intersinus septum is usually complete A larger frontal sinus may occupy both frontal regions, and the smaller one may lie anterior or posterior to it. Agenesis of the frontal sinus is a rare anomaly but duplication and triplication is common. Congenital dehiscences in the osseous walls, especially in the orbital portion, do occur (38) and the importance of these defects in regard to the spread of infection to the orbit or meninges is apparent.

Bony septa frequently project inward from the walls of the frontal sinus and divide it incompletely into compartments. These projections must be leveled during surgery to assure complete removal of mucous membrane.

Orbital and temporal recesses may be extensive Whitnall (39) described a frontal sinus which undermined the orbital roof to the apex. These recesses are sometimes ignored and considered a cause for surgical failure

The squama of the frontal bone is very thick and has diploic tissue with marrow between two compact laminae, but the orbital portion is thin and composed only of compact bone Thus the anterior wall of the frontal sinus is thick like the squama, and the floor and posterior wall are thin. The floor is the site of the earliest external sign of inflammation in acute suppurative sinusitis, and it is also the preferred area for entering the sinus, being most dependent and containing no diploic bone The anatomic landmark for surgical intervention is the junction of the articulation of the nasal bone frontal process of the maxilla and the frontal bone

After the sinus is entered, one must be cautious with dissection over the dorsomedial wall for the olfactory fissure occasionally projects into the sinus as a bulla in this area. Another area of concern is the posterior wall of the nasofrontal duct beneath which the anterior edge of the cribriform plate lies. Frequently a bulge into the lower lumen of the sinus is caused by a frontal bullar cell, and occasionally a nest of cells may be present in this area

The position of the ostium in the floor is of practical importance for when the istium is posteriorly placed the pathway into the nose is tortuous with encroachment by frontal recess or infundibular cells, but when it lies anteriorly the pathway is vertically direct into the anterior middle meatus (40) It has been stated that the duct leads into the frontal recess in 67% of patients, the ethmoidal infundibulum in 30% and an ethmoidal cell expansion in 3% (41) A narrow middle meatus from a cellular or hypertrophied middle turbinate may also compromise the nasal drainage route

The mucous membrane of the frontal sinuses is composed of a stratified ciliated columnar epithelium overlying a delicate basal membrane and thin tunica propria (42, 43) Although continuous with the nasal fossa, it is much thinner and contains fewer glands and elastic fibers. Numerous arteries and veins lie in the stroma The tunica is firmly adherent to the underlying periosteum, making dissection of the mucoperiosteum a necessity when removing the membrane during surgery

The arterial blood supply to the frontal sinus is the anterior and posterior ethmoidal branches of the ophthalmic artery Ramifications of these vessels form a close plexiform network in the mucous membrane Veins also form a plexus and end in the superior ophthalmic vein although a few may communicate intracranially through the diploic system, foramina in the cribriform plate, or through a patent foramen cecum These anastomoses have obvious significance in the pathogenesis of intracranial complications resulting from frontal sinusitis.

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medially The axis of the ethmoid labyrinth intersects with the optic canal, and this is the site where the optic nerve is likely to be injured. Also the roof, medial, and lateral walls of the canal may be thinned out by extensions of the sphenoid or posterior ethmoid cells further predisposing the nerve to injury during surgery Westlake (45) first reported this relationship in 1923

IV Physiologic Principles

McDonald (46) and Heetderks (47) observed the nasal efficiency in filtration, heating and humidification of inspired air These functions are impaired when vasomotor control is interrupted by exposure and viral invasion. There is an ischemia of the mucous membrane with a deficient mucus blanket and ciliary action. The resulting obstruction to aeration and discharge predisposes to bacterial invasion and the production of a suppurative sinusitis.

The ciliated mucous membrane with its secreting glands and overlying blanket of mucin must be regarded as a membrane of defense capable of returning to a normal state under favorable conditions (48, 49)

Hilding (49) has demonstrated that the mucus blanket is propelled by the cilia in a very consistent spiral direction around the sinus to discharge through the nasofrontal duct into the nose. The force is considered optimal at 5 g/cm² with the weight load increasing the activity of the cilia. The speed of the cilia in man is about 250 cycles per minute with the motion of the blanket and force becoming greater as the ostium is approached (50)

The ostium and its surrounding pathway into the nose must remain patent for normal aeration and cilial function. Positive intranasal atmospheric pressure with an occluded nasofrontal duct will prevent discharge of sinus contents by gravity Hence if aeration can be established by conservative means, drainage is facilitated by cilial action, and the infection may be eradicated. Local and systemic medical therapy will accomplish these objectives in most acute diseases. However at times in subacute or early chronic sinusitis, minor surgical procedures are also indicated. The goal is to establish drainage with minimal trauma to the nasofrontal duct area.

Excessive or prolonged use of local decongestants may produce a superimposed rhinitis medicamentosa. Lillie (51) observed the congestion of the nasal mucosa after prolonged irrigations at surgery and Stark (52) demonstrated the destructive histologic changes in rabbits after irrigations with tap water saline, and 2% sodium chloride Epithelial cells were distended and cilia were absent. The mucus layer and tunica were infiltrated with polymorphonuclear cells and the blood vessels were dilated Injury may also be induced by nasal packing and instrumentation with erosion or avulsion of inflamed nasal mucosa.

Formerly surgery upon the frontal sinus was followed by a high incidence of recurrent disease. In an attempt to discover the causes of surgical failure, Hilding (53) removed the intersinus septum and strips of mucous membrane from the frontal sinuses of dogs and found that high ridges and diaphragms of scar tissue formed at the excision sites. In another series of experiments designed to determine the nature of regenerated mucous membrane Hilding (53) found that in complete removal the sinus often filled with scar tissue and in partial removal an abortive cystic epithelial lining reformed. These findings differ from those of Coates & Ersner (55) who previously had noted complete regeneration in one dog after radical removal of the mucous membrane. McGregor (56) reported on a human specimen with normal lining of the frontal sinus six months after operation. Walsh (57) in further

The general sensory nerve supply to the frontal sinus is the anterior ethmoidal nerve, a branch of the ophthalmic division of the trigeminal nerve Autonomic innervation is by parasympathetic fibers from the sphenopalatine ganglion and sympathetic fibers from the carotid plexus

Not infrequently ethmoidectomy may accompany frontal sinus surgery and several anatomic landmarks should be stressed Attachments of the middle and superior turbinates form the medial boundary of the ethmoid labyrinth The cribriform plate is located medially and preservation of the turbinates protects it The lamina papyracea of the medial orbital wall forms the lateral boundary Anterior and posterior ethmoidal vessels are encountered along the junction of the superior and medial orbital wall

Structures of the medial orbital wall lie in close proximity to the fronto-ethmoid incision, and a discussion of anatomical landmarks in this area is warranted The septum orbitale is a thin membrane of connective tissue which extends from the orbital to the palpebral margins and forms a barrier between the lids and orbital contents A frontal incision placed too low will perforate this partition and orbital fat will herniate through the opening.

The medial palpebral ligament is palpable as a horizontal cord like band of connective tissue connecting the tarsi to the lacrimal crest It lies in front of the upper half of the lacrimal sac, and its proximity to the fronto-ethmoid incision should be recognized

The lacrimal canaliculi are two minute canals connecting the lacrimal puncta to the lacrimal sac They are each 10 mm long with a short vertical part deep to the puncta and a longer horizontal part running along the medial upper and lower lid margins An incision placed along the orbital rim will avoid these structures

The lacrimal sac lies beneath the periorbita in the lacrimal fossa on the medial margin of the orbit. The nasolacrimal duct is a continuation of the sac lying in the osseous nasolacrimal canal and opening into the inferior meatus of the nose The fundus of the lacrimal sa cis often seen in the lower part of the incision just anterior to the posterior lacrimal crest This crest forms the anterior limit of the external ethmoidectomy Proceeding forward on the medial side of the upper half of the lacrimal fossa one will encounter one or two cells of the anterior ethmoid group known as the lacrimoethmoidal cells (39) Although the anterior ethmoidal cells may be approached externally through this route the operation should be completed through the intranasal approach

The fovea trochlearis is a small round pit in the bone at the anteromedial angle of the roof of the orbit about 5 mm from the margin The trochlea or pulley of the superior oblique muscle is a finely grooved, curved plate of fibrocartilage about 4 mm long and 6 mm broad The edges are attached to the fovea by fibrous tissue completing the tube through which the superior oblique tendon slides. If the frontal periosteum is reapproximated after the bone removal, no impairment of extraocular muscle function will result The trochlea attached to periosteum is restored to its normal position

The inferior oblique muscle originates from a shallow depression on the inferior medial orbital wall just lateral to the opening of the nasolacrimal canal It passes laterally and posteriorly into the orbit as a flat band beneath the inferior rectus and inserts into the posterolateral hemisphere of the eyeball The proximity of this muscle to the ethmoidal cells in this area should be recognized

At the apex of the orbit the optic nerve is covered by the dural sheath and closely surrounded by the recti muscles at their origin from the annulus of Zinn The ophthalmic artery lies on the lateral aspect of the nerve posteriorly at the apex

The optic foramen is located at the apex of the roof of the orbit and opens into the optic canal formed by the two roots of the lesser wing of the sphenoid bone It is 4–9 mm in length and its axis is directed posteriorly and

and the bony opening was occluded with bone chips or surrounding soft tissue. The cavity was left to be spontaneously obliterated in nine cases. Abdominal fat was inserted in one highly pneumatized cavity

F COMPLICATIONS

The majority of complications encountered in this series were ocular (Table VIII). Supraorbital nerve injury occurred in three patients during exposure of highly pneumatized frontal sinuses. Anesthesia was temporary in two patients where the nerve was compressed by retractors and permanent in one patient where the nerve was divided.

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Inferior oblique palsy	1
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Dural laceration	1
Meningitis	1
Frontal lobe abscess	1
Cerebrospinal fluid rhinorrhea	1

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One patient with a frontal lobe abscess most likely had the abscess prior to sinus surgery for it appeared chronic upon neurosurgical intervention two weeks later We have encountered the reverse situation where asymptomatic frontal sinusitis was discovered by the neurosurgeon during operation for a symptomatic frontal lobe abscess.

G RECURRENCE RATE

Most recurrences were associated with the minor procedures of incision, drainage and trephine. Reconstructions of the nasofrontal duct were complete failures in our series. Extended trephine and nasofrontal duct stenting procedures reduced the recurrence rate by nearly 50% The obliteration, however has been a highly successful operation with no recurrences to date.

All patients were followed closely for at least one year after surgery Recurrent or continued disease usually manifested itself within that period of time. One exception was one patient with a latent period of 15 years. For the obliteration procedure the minimum follow-up time was six months and the maximum time was six years.

The general sensory nerve supply to the frontal sinus is the anterior ethmoidal nerve, a branch of the ophthalmic division of the trigeminal nerve Autonomic innervation is by parasympathetic fibers from the sphenopalatine ganglion and sympathetic fibers from the carotid plexus

Not infrequently ethmoidectomy may accompany frontal sinus surgery and several anatomic landmarks should be stressed Attachments of the middle and superior turbinates form the medial boundary of the ethmoid labyrinth. The cribriform plate is located medially and preservation of the turbinates protects it The lamina papyracea of the medial orbital wall forms the lateral boundary Anterior and posterior ethmoidal vessels are encountered along the junction of the superior and medial orbital wall.

Structures of the medial orbital wall lie in close proximity to the fronto-ethmoid incision, and a discussion of anatomical landmarks in this area is warranted The septum orbitale is a thin membrane of connective tissue which extends from the orbital to the palpebral margins and forms a barrier between the lids and orbital contents. A frontal incision placed too low will perforate this partition and orbital fat will herniate through the opening

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Nonspecific changes such as increased density of the sinus lumen, loss of the mucoperiosteal line and sclerosis around the margins were frequently noted

When radiopaque dye could be instilled into the frontal sinuses, diffuse mucosal hypertrophy could be demonstrated. However the technical difficulties encountered with an occluded middle meatus and rapid return of the dye into the nose limited the value of this procedure.

Tomography and more recently polytomography demonstrated mucosal changes and bone dehiscence not apparent with conventional views

Table III. *Radiology*

Specific changes	17
Nonspecific changes	16

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Bone pathology noted in half of the patients included osteoporosis with dehiscence of the frontal floor and osteitis with increased bone density Both changes occurred simultaneously in patients with chronic disease (Table VI) Only two cases of osteomyelitis were seen, and in each the process was localized in the anterior wall and was arrested by limited bone removal. No loculated abscesses, draining sinuses or sequestrated bone, so characteristic of osteomyelitis elsewhere were encountered.

The cell types in the four malignant tumors were squamous cell (2) reticulum cell (1) and basal cell (1) Considerable inflammatory reac

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Acute suppurative sinusitis	13
Pyocele	4
Mucocele	4
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experiments on dogs demonstrated rapid regeneration of normal mucosa throughout the sinus when only the lining of the nasofrontal duct was preserved Although inconclusive these various observations tend to support the ability of the frontal sinus mucosa to regenerate and call for a conservative approach to surgical therapy in acute, subacute and early phases of chronic disease

When more radical surgery is indicated, Van Alyea (41) has cautioned against procedures which direct air streams into the ostia or sinus cavities Disruption of intranasal anatomy and physiology is clearly demonstrated by the crusting, atrophy and ulceration often apparent at the site of an intranasal ethmoidectomy or turbinate resection These patients may have more symptoms related to the surgery than to the primary disease The extranasal approach to the fronto-ethmoid sinuses therefore appears more logical since important normal intranasal function is maintained Also the irreversibly damaged sinuses can be exenterated and partially separated from the nasal cavity by this procedure

V Review of Cases

Records of 33 patients operated upon between 1946 and 1968 were reviewed (Table I) Inflammation was present in 31 Two cases of osteomas were not secondarily infected. Four patients had malignant neoplasms Three tumors presented intranasally and involved the ethmoid and frontal sinuses The fourth tumor was a basal cell carcinoma of the skin adjacent to the inner canthus of the eye lids which eroded the bone of the lateral nasal wall and extended into the ethmoid and frontal sinuses. There was evidence of suppuration with all of the tumors

In the series there were 26 males and 5 females and the age range varied between 18 and 66 The predominant veteran population explains this distribution

A ETIOLOGY

Local etiologic factors considered contributory to the development of frontal sinusitis are difficult to evaluate (Table II) A significant obstructive deviation of the nasal septum was present in 25% of cases. Hypertrophied anterior middle turbinates and anterior middle meatal polyps were found in 20% Frontal sinus fracture appeared to be a significant predisposing factor in 33% of this series Associated maxillary and ethmoid sinusitis were found in half of the patients. However definitive treatment of the maxillary or ethmoid sinusitis did not seem to influence the clinical course of the frontal sinus disease Specific allergic etiology demonstrated by nasal eosinophilia, positive skin testing and favorable response to desensitization was found in less than 10% of patients No local etiologic factors could be determined in 20%

Table I *Stage of disease*

Acute	15
Subacute	7
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Frontal projections of Caldwell & Waters were of value in demonstrating sinus size configuration, and presence of supraorbital ethmoid or frontal bullar cells. Varying degrees of opacification were noted, but definite indications of activity of the disease process were present in only half of the patients (Table III)

Discrete bony changes such as erosion of the sinus floor and anterior plate or mottling

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tion surrounded the neoplastic cells and several biopsies were necessary to establish a histologic diagnosis The neoplasms grossly presented as granular polypoid or ulcerative lesions

E. SURGERY

Indications for surgery were lack of response to medical therapy persistent localizing signs, or signs of impending intracranial complications

Operative procedures included incision and drainage simple or extended trephination and obliteration by osteoplastic flap or frontal floor approach (Table VII)

Incision and drainage was performed on three patients One with an initial attack of frontal sinusitis had a subperiosteal abscess with no gross evidence of bone erosion The other two cases with secondary attacks, had mucocele pyocele formation and erosion of the sinus floor

Trephination was considered the primary procedure for acute eroding sinusitis whenever drainage was necessary Many of our cases fell into this category with multiple procedures performed in some patients

Extended trephination was also performed frequently when reoperation was indicated. An opening in the frontal sinus floor was enlarged to adequately inspect the mucosal lining and the posterior sinus plate Hyperplastic and polypoid mucosa was removed but a cuff was usually spared at the nasofrontal duct orifice Margins of eroded bone of the floor anterior or posterior wall, were removed until normal appearance and consistency were apparent. Granulations were removed from the dura beneath a dehiscent posterior plate in two patients

Several attempts were made at reconstruction of the nasofrontal duct, with mucosal and skin grafts These patients formed strictures and had recurrent frontal sinusitis

Polyethylene and silastic tubes were utilized as stents in the nasofrontal duct in seven patients. The initial experience was encouraging but recurrent disease was frequent.

Sinusotomy in the four patients with malignant tumors was considered a diagnostic and therapeutic procedure Extent of the disease was determined and all the gross tumor was removed A widely patient intranasal communication was established to facilitate drainage during postoperative radiation therapy

Obliteration was performed only in the quiescent or chronic stage of disease The osteoplastic flap was used in the first two patients, but the frontal floor approach was used for the subsequent eight Mucosa and bony septa were meticulously removed from the sinus lumen. The cuff of mucosa in the nasofrontal duct was excised well into the nose

Table VII *Operations*

Procedure	No cases	Recurrence rate
Incision drainage	3	100
Trephine	25	86
Extended trephine	11	45
Reconstruction nasofrontal duct	3	100
Obliteration	10	0

(Follow-up time—6 months to 20 years)

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The majority of complications encountered in this series were ocular (Table VIII) Supraorbital nerve injury occurred in three patients during exposure of highly pneumatized frontal sinuses. Anesthesia was temporary in two patients where the nerve was compressed by retractors and permanent in one patient where the nerve was divided.

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tion surrounded the neoplastic cells and several biopsies were necessary to establish a histologic diagnosis The neoplasms grossly presented as granular polypoid or ulcerative lesions

E SURGERY

Indications for surgery were lack of response to medical therapy persistent localizing signs, or signs of impending intracranial complications

Operative procedures included incision and drainage, simple or extended trephination, and obliteration by osteoplastic flap or frontal floor approach (Table VII)

Incision and drainage was performed on three patients One with an initial attack of frontal sinusitis had a subperiosteal abscess with no gross evidence of bone erosion The other two cases, with secondary attacks, had mucocele pyocele formation and erosion of the sinus floor

Trephination was considered the primary procedure for acute eroding sinusitis whenever drainage was necessary Many of our cases fell into this category with multiple procedures performed in some patients

Extended trephination was also performed frequently when reoperation was indicated An opening in the frontal sinus floor was enlarged to adequately inspect the mucosal lining and the posterior sinus plate Hyperplastic and polypoid mucosa was removed but a cuff was usually spared at the nasofrontal duct orifice Margins of eroded bone of the floor anterior or posterior wall were removed until normal appearance and consistency were apparent Granulations were removed from the dura beneath a dehiscent posterior plate in two patients

Several attempts were made at reconstruction of the nasofrontal duct with mucosal and skin grafts These patients formed strictures and had recurrent frontal sinusitis

Polyethylene and silastic tubes were utilized as stents in the nasofrontal duct in seven patients. The initial experience was encouraging but recurrent disease was frequent

Sinusotomy in the four patients with malignant tumors was considered a diagnostic and therapeutic procedure Extent of the disease was determined and all the gross tumor was removed A widely patient intranasal communication was established to facilitate drainage during postoperative radiation therapy

Obliteration was performed only in the quiescent or chronic stage of disease The osteoplastic flap was used in the first two patients, but the frontal floor approach was used for the subsequent eight. Mucosa and bony septa were meticulously removed from the sinus lumen. The cuff of mucosa in the nasofrontal duct was excised well into the nose

Table VII *Operations*

Procedure	No cases	Recurrence rate
Incision drainage	3	100
Trephine	25	86
Extended trephine	11	45
Reconstruction nasofrontal duct	3	100
Obliteration	10	0

(Follow up time—6 months to 20 years)

and the bony opening was occluded with bone chips or surrounding soft tissue. The cavity was left to be spontaneously obliterated in nine cases. Abdominal fat was inserted in one highly pneumatized cavity

F COMPLICATIONS

The majority of complications encountered in this series were ocular (Table VIII) Supraorbital nerve injury occurred in three patients during exposure of highly pneumatized frontal sinuses. Anesthesia was temporary in two patients where the nerve was compressed by retractors and permanent in one patient where the nerve was divided.

Superior oblique palsy complicated one fronto-ethmoid exenteration The trochlea was displaced from its fossa and not replaced. Impaired function was permanent and required a recession of the inferior oblique muscle

Recently we encountered an inferior oblique muscle paralysis following a fronto-ethmoid exenteration. The resulting hypotropia and vertical diplopia subsided within three months.

Optic neuritis occurred in one patient following a fronto-ethmoid exenteration. Recovery occurred within two months. It is probable that the optic nerve was contused by retraction during the posterior ethmoidectomy

The fundus of the lacrimal sac was lacerated in one patient. The defect was sutured, and there was no epiphora.

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Table VIII. *Complications*

Supraorbital anesthesia	3
Superior oblique palsy	1
Inferior oblique palsy	1
Optic neuritis	1
Lacrimal sac laceration	1
Dural laceration	1
Meningitis	1
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One patient with a frontal lobe abscess most likely had the abscess *prior to sinus surgery* for it appeared chronic upon neurosurgical intervention two weeks later We have encountered the reverse situation where asymptomatic frontal sinusitis was discovered by the neurosurgeon during operation for a symptomatic frontal lobe abscess.

G RECURRENCE RATE

Most recurrences were associated with the minor procedures of incision, drainage, and trephine Reconstructions of the nasofrontal duct were complete failures in our series. Extended trephine and nasofrontal duct stenting procedures reduced the recurrence rate by nearly 50% The obliteration, however has been a highly successful operation with no recurrences to date

All patients were followed closely for at least one year after surgery Recurrent or continued disease usually manifested itself within that period of time. One exception was one patient with a latent period of 15 years For the obliteration procedure the minimum follow-up time was six months and the maximum time was six years.

Table VI *Bone pathology*

Osteitis	19
Osteoporosis	15
Osteomyelitis	4
Osteoma	3
No specimen	9

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VI Discussion

Frontal sinusitis is infrequent today The lower incidence of this disease as compared with maxillary sinusitis may be due to the natural dependent drainage Also antibiotic therapy has reduced the incidence of acute complicated sinusitis and allowed limited operations to be performed in the chronic phase of the disease (58) However with the less accurate and technically more difficult means of establishing a diagnosis of frontal sinusitis by irrigation and Proetz displacement therapy it is surmised that there are many cases of quiescent chronic suppurative disease that are overlooked Reluctance to operate because of the previous high recurrence and complication rates may also explain the infrequent reports in the literature

Significant etiologic factors suggested in our series were frontal sinus fractures, and coexisting maxillary and ethmoid sinus disease Morrison (59) previously pointed out that chronic frontal sinusitis seldom occurs as a single clinical entity unless caused by trauma Work (60 61) also noted this relationship to trauma

Conventional radiologic projections of Caldwell & Waters revealed general configuration, opacity of sinus lumen and sclerosis of bony walls Polytomography has aided in diagnosis of activity with visualization of the details of mucosal thickening and bone erosion In most of the recent cases operated upon the clinical impressions of activity were confirmed at surgery

Staphylococcus aureus and Diplococcus pneumoniae comprised 80% of the pathogens isolated in this series These findings are similar to those listed by Eggston & Wolff (62) However the organisms could often not be identified in the acute stage of disease when specific antibiotic therapy was instituted Most cultures were obtained from spontaneous intranasal drainage during resolution or from the lumen when the sinus was opened externally This exudate was frequently sterilized by the previous antibiotic therapy

Pathologic classifications of sinusitis suggested by Hajek (63) Eggston (64) and Schall (65) stressed the stage of disease, degeneration and regeneration Proetz (66) previously noted that these disease processes occurred simultaneously with areas of normal epithelium persisting in severe sinusitis Specimens in this series revealed similar findings No polyps were found in our specimens. Dixon (67) previously commented on similar experience Perhaps the anatomic configuration of the frontal sinuses is not conducive to polyp formation

Mucoceles and pyoceles were encountered in our series Finck (68) believed the mucocele formed when the sinus ostium was blocked and goblet cells continued to secrete mucus. Turner (69) stressed that chronic inflammation was necessary for their formation and that their presence implied irreversible mucosal changes It seems likely that partial obstruction of the nasofrontal duct predisposes to goblet cell proliferation in the frontal sinus because Hilding (70) noted a great increase in these cells in the occluded nostrils of dogs and rabbits In our series either trauma or surgery preceded the development of all mucoceles and pyoceles

Bone may be as vulnerable as soft tissue to bacterial agents Osteoporosis and osteitis were the most frequent pathologic findings. Osteoporosis may occur as a result of osteoclasis or halisteresis processes causing the bone to become thinner and the trabulae atrophic (71) In the osteitic or osteoblastic changes the bone density increases There is no exact correlation between bone and soft tissue disease although osteoporosis with absorption of adjacent bone is more often associated with mucoceles and osteitis commonly accompanies chronic fibrotic sinusitis.

In frontal osteomyelitis the causative organism spreads along the venous channels in trabecular or lamellar bone and in marrow of diploic bone. Infection is usually first manifested at the junction of the anterior and posterior walls where the numerous channels in cancellous and diploic bone favor dissemination. Mosher (72) demonstrated the pathogenesis of osteomyelitis showing infected thrombi extending from the veins of the sinus mucosa to the diploe of the frontal bone. The gravity of this complication has been well documented by McNalley & Stuart (73) where subdural and brain abscess, cerebral venous thrombosis, and meningitis were the sequelae. The low incidence of osteomyelitis in this series was probably due to the intensive antibiotic therapy and relatively early surgical intervention in these patients.

Most tumors of the nose and sinuses are malignant. The squamous cell epithelioma is most common according to New & Erich (74). In the highly anaplastic variety there is disagreement in regard to pathologic classification. Godtfredson (75) maintains that many of these rightfully belong in the reticulum cell sarcoma group. Eggston & Wolff (76), on the other hand, believe that fibrosarcoma is the most common type of mesenchymal malignancy in the nose and accessory sinuses. There have also been differences of opinion regarding the cell types in our series.

Minor intranasal operative procedures such as irrigation, infracture of the middle turbinate, polypectomy, penetration of encroaching cells, and resection of the anterior middle turbinate are indicated as adjunct to medical therapy in acute and early chronic sinusitis. Pratt (77) described an intranasal approach to the frontal sinus through the bulla ethmoidalis by removal of sufficient bone, enlargement of the opening medially to the intrasinus septum, and removal of diseased mucosa with a ring curette. However, it is unlikely that any medical or intranasal surgical procedure will cure a well-established chronic infection (59, 78).

Williams & Mousel (79) listed a number of surgical principles to be followed in sinus surgery. Direct vision with adequate exposure and drainage along normal routes were considered important. Elimination of multiple cavities and the preservation of functioning nasal anatomy were also mentioned. They gave criteria for choosing between the external or internal approach to the sinuses. The external route was recommended for exteriorized disease, excessive pneumatization, a narrow ethmoid labyrinth, bony wall sclerosis, and secondary procedures. Generally the external approach has been advocated and favored because it is more direct, yielding better visualization, and there is less destruction to nasal physiology. These reasons appear valid to the author.

Trephination is a limited operation usually reserved for acute suppurative disease unresponsive to medical therapy. It is the primary procedure indicated in acute eroding sinusitis when drainage is necessary. The opening may be enlarged for a better view of the sinus interior.

In the extended trephination the opening in the sinus floor is enlarged to adequately inspect the mucosal lining and posterior sinus plate. Mucosa is removed when it appears irreversibly hyperplastic or polypoid, but a cuff of mucosa is spared at the nasofrontal duct orifice. Margins of eroded bone are removed from the anterior or posterior plates until normal appearing bone is noted. Granulations are removed from the dura when present. This procedure may be indicated in subacute or early chronic disease.

Prostheses, mostly polyethylene tubes, as stents for the nasofrontal duct were utilized in seven cases as recommended by Hugenberg & Williams (24) and Goodale (80). Our initial experience was encouraging but the tubes became plugged with dried secretions and several patients had an acute exacerbation of sinusitis with the patent tubes in place.

Reconstruction of the nasofrontal duct, as recommended by Sewall (18), Hoople (81), Boyden (20) and Ogura et al. (21), failed in

three instances Strictures formed and recurrent frontal sinusitis occurred

There was reluctance to attempt the radical exenterations of Killian (11) Jansen (13) and Lynch (14) Anderson (82) earlier had noted the frequent failures due to incomplete surgery and closure of the frontonasal opening. McNalley & Stuart (73) stated that only three of fifteen operated patients remained symptom free Also Goodale (83) in a review of 82 patients found a recurrence rate of over 50% Thus combined external and internal frontal operations have fallen into disrepute because of the high incidence of residual disease and morbidity

One indication for these extensive procedures is a malignancy of the nose and sinuses An exploration is necessary to determine the extent of the disease facilitate removal of the bulk of the tumor and establish a nasal drainage route to eliminate the products of cellular disintegration produced by subsequent radiotherapy

The obliteration originally described by Kuhnt (3) led to recurrent disease and was markedly deforming However Goodale (84) in 1955 recommended a modification of the procedure advising removal of the anterior and inferior walls the sinus mucosa a base leveling of the septa and a complete ethmoidectomy Disfigurement was corrected by autogenous bone grafting In 1957 Goodale (85) reported favorable results with obliteration using a tissue implant of abdominal fat, and in 1965 he (33) emphasized the importance of removal of the mucous membrane from the nasofrontal duct and sinus cavity and the occlusion of the nasofrontal duct. He noted spontaneous obliteration by fibrous tissue and bone and believed that adipose tissue delayed or prevented osteogenesis Skolnik et al (86) cautioned that the obliteration procedure was contraindicated in acute disease where drainage is necessary and it has been our policy to perform the operation only in the chronic stage of disease

Mucosa and bony septa are meticulously removed from the sinus lumen The anterior plate is removed and laterally to facilitate exposure A cuff of mucosa of the nasofrontal duct is excised well into the nasal cavity and the opening is occluded with bone chips or soft tissue On several occasions when the lateral nasofrontal duct and ethmoid cells were eroded the communication between the nasal cavity and exenterated sinus was large An enlarged opening into the nose also resulted when the ethmoidectomy was combined with the frontal exenteration without preservation of the lateral wall of the nasofrontal duct. Temporalis fascia, either folded or in sheet form provided a satisfactory occlusion in these cases

The osteoplastic anterior wall approach to the frontal sinus gives wide exposure and minimal deformity Goodale & Montgomery (31 32) in 1958 and 1964 reported successes with it. However Alford et al (87) in 1965 listed acute infections, fractures osteomyelitis, and previous operations with extensive periosteal elevation as contraindications to the u e of the osteoplastic flap In many of these cases the frontal floor approach would appear applicable

The osteoplastic flap was utilized on the first three obliteration operations but the frontal floor approach was used on the subsequent procedures It appears that this route is satisfactory for most obliterative procedures. In the poorly pneumatized sinus the frontal floor removal offers adequate exposure For the highly pneumatized sinuses the anterior wall can be partially removed above and laterally without causing a notable external deformity The use of a mirror an angulated drill, and the operating microscope facilitate and ascertain removal of mucosa from the recesses

Complications related to surgery for frontal sinusitis are not infrequent but the incidence has been reduced in recent years by antibiotics and refinements in the operative procedures In the early twentieth century disease was more likely to be eradicated by extensive procedures

with removal of normal tissue adjacent to an inflammatory process (88 89 90)

Ocular complications are common because of the proximity to the operative site (40) Chronic upper lid edema is due to severance of lymphatics by an elongated curvilinear incision Edema also occurs following faulty closure of the frontal incision when the scar is adherent to underlying bone. Hematoma is related to inadequate hemostasis in this highly vascular area. Wound infection results from tissue ischemia and contamination by Staphylococcus aureus, the nasal vestibule being the probable source of this pathogen.

The supraorbital nerve may be compressed by retraction or severed by the incision with resulting paresthesia or anesthesia. This complication is uncommon and can usually be avoided

An incision made too low in the upper lid may sever the levator muscle with resulting ptosis. Careful palpation of the bony landmarks of the frontal floor will prevent this complication.

Extraocular muscles may be injured. The trochlea and tendon of the superior oblique or the superior medial orbital wall are most vulnerable Killian (11) avoided damage to the trochlea by removal of the frontal sinus floor from above and stated that fibrous strands connected to the supraorbital ridge helped maintain its normal position. Kuhnt (3) had noted earlier that displacement of the trochlea caused diplopia which subsided in a short period of time. Our experience has been similar Subperiosteal dissection without laceration and accurate reapproximation should prevent any palsy

The inferior oblique muscle can also be injured on the inferior medial orbital wall during a fronto-ethmoid exenteration. This muscle origin is usually just lateral to the bony opening of the nasolacrimal canal, and in this location it should not be injured by an ethmoidectomy However Whitnall (91) in a study of 100 orbits, found that the origin was 2 to 7 mm higher in 55 Here it lies in the proximity of the ethmoid dissection. Thus, anomalous origin appears to be the best explanation for this complication. If the orbital periosteum is inadvertently opened during curettement of the fronto-ethmoid cells, the medial and superior rectus muscles may be directly lacerated. The more remote possibility of perforation of the eyeball should also be mentioned.

The lacrimal sac may be damaged by an inferiorly placed incision or by curettement of the ethmoid cells adjacent to the posterior lacrimal crest. However the fundus of the sac should be identified as a bluish dome-shaped structure 4–5 mm in diameter lying in the lacrimal fossa.

Avulsion or severance of the medial canthal ligament results in the lateral displacement of the inner canthus. If severed, it can be reapproximated by a nonabsorbable suture If avulsed with no bony attachment remaining, burr holes are made in the lateral nasal wall to anchor the ligament to its former site

The optic nerve may be injured in a posterior ethmoidectomy where the distance separating ethmoid cells from the optic foramen is only 5 mm. Trauma is effected by too vigorous retraction on the overlying periosteum or by laceration of it during curettement of the cells. Obviously extreme caution should be exercised in this area.

Cerebrospinal fluid leaks are produced by trauma perforating the anterior fossa dura beneath the posterior sinus wall or the cribriform plate beneath the posterior nasofrontal duct. Meningitis, brain abscess, or cerebral venous thrombosis are possible complications from such an exposure in an infected sinus, and antibiotic prophylaxis is indicated

Calvet (92) believed that intracranial infection could come from sinuses that were not infected, and Work (60) recommended ablation after compound fractures because of these serious complications McHugh (93) found dural lacerations beneath the displaced bone fragments away from the site of the fracture lines Dural tears can be sutured with small lacrimal needles, and dural defects may be covered with a fascial graft.

Osteomyelitis has been reported following frontal sinus surgery (94) Schenk (95) emphasized that antibiotics and chemotherapy have reduced the incidence and severity of the disease This rare complication is more likely if diploic bone is exposed to suppuration The possibility of overlooking early bone involvement at the primary operation must be considered. Williams (79) stated that osteomyelitis begins in the cancellous bone of the nasion and spreads to the frontal bone by thrombophlebitis of the vein of Breschet a large fairly constant vessel passing in this region He believed the Killian procedure which interrupted this communication prevented the disease from reaching the frontal bone

It appears that current surgical refinements, with separation of the frontal and ethmoid procedures when indicated and the utilization of obliteration have considerably reduced the operative complication rate A recent series of 100 cases reported by Zonis, Montgomery & Goodale (94) included only five secondarily infected hematomas one thrombophlebitis and nonfatal pulmonary embolism and one lacerated anterior fossa dura with cerebrospinal fluid leak As a comparison McNalley & Stuart (73) in a 30 year review reported in 1954 listed an overall complication rate of 60% in acute and 40% in chronic frontal sinusitis

All previous operations from the simple trephine to the radical Jansen Ritter & Lynch procedures were followed by a high incidence of *recurrent disease* The enlarged debrided nasofrontal duct became a strictured nonfunctioning communication More physiologic nasofrontal duct reconstructions with mucosa and skin grafts reduced the recurrence rate considerably but failures were frequent in larger series. Strictures prevented adequate drainage from above and predisposed to ascending infection from below

With acknowledgement of failure to maintain a functional nasofrontal duct and promote regeneration of normal sinus mucosa removal of all sinus mucosa and permanent occlusion of the nasal opening seems to be the only alternative procedure The obliteration, eliminating the exenterated sinus as a functioning organ has produced better results than any previous operation In the large series reported by Zonis, Montgomery & Goodale (94) there was only a 3% failure rate This smaller series reported compares favorably with no recurrences being observed at this time

Summary and Conclusions

The history of frontal sinus surgery is reviewed and trends in conservative and radical surgical procedures are documented Revival of previously advocated operations with current modifications is noted.

Surgical anatomy of the frontonasal area is reviewed and certain variations and landmarks are stressed

Physiologic principles related to frontal sinus surgery are discussed

Thirty-one patients with frontal sinusitis operated upon over a period of 20 years are reviewed. The following pertinent observations are noted

1 Etiologic factors of significance are associated maxillary and ethmoid sinusitis and frontal sinus trauma

2 Radiologic interpretation of activity of disease is difficult with conventional views, but polytomography often reveals specific changes

3 Staphylococcus aureus and Diplococcus pneumoniae are the most frequent pathogens cultured

4 Pathologic findings often demonstrated are irreversible mucosal disease and bone absorption

5 Surgical procedures of incision, drainage and trephine lead to a high recurrence rate

6 The obliteration procedure, utilizing the osteoplastic flap or frontal floor approach, reduces the recurrence rate and seems to be the procedure of choice for chronic recurrent frontal sinusitis.

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Osteomyelitis has been reported following frontal sinus surgery (94) Schenk (95) emphasized that antibiotics and chemotherapy have reduced the incidence and severity of the disease This rare complication is more likely if diploic bone is exposed to suppuration The possibility of overlooking early bone involvement at the primary operation must be considered Williams (79) stated that osteomyelitis begins in the cancellous bone of the nasion and spreads to the frontal bone by thrombophlebitis of the vein of Breschet a large fairly constant vessel passing in this region He believed the Killian procedure which interrupted this communication prevented the disease from reaching the frontal bone

It appears that current surgical refinements, with separation of the frontal and ethmoid procedures when indicated and the utilization of obliteration have considerably reduced the operative complication rate A recent series of 100 cases reported by Zonis, Montgomery & Goodale (94) included only five secondarily infected hematomas one thrombophlebitis and nonfatal pulmonary embolism, and one lacerated anterior fossa dura with cerebrospinal fluid leak As a comparison McNalley & Stuart (73) in a 30 year review reported in 1954 listed an overall complication rate of 60% in acute and 40% in chronic frontal sinusitis

All previous operations from the simple trephine to the radical Jansen Ritter & Lynch procedures were followed by a high incidence of recurrent disease The enlarged debrided nasofrontal duct became a strictured nonfunctioning communication More physiologic nasofrontal duct reconstructions with mucosa and skin grafts reduced the recurrence rate considerably but failures were frequent in larger series. Strictures prevented adequate drainage from above and predisposed to ascending infection from below

With acknowledgement of failure to maintain a functional nasofrontal duct and promote regeneration of normal sinus mucosa, removal of all sinus mucosa and permanent occlusion of the nasal opening seems to be the only alternative procedure. The obliteration, eliminating the exenterated sinus as a functioning organ has produced better results than any previous operation In the large series reported by Zonis Montgomery & Goodale (94) there was only a 3% failure rate This smaller series reported compares favorably with no recurrences being observed at this time

Summary and Conclusions

The history of frontal sinus surgery is reviewed and trends in conservative and radical surgical procedures are documented. Revival of previously advocated operations with current modifications is noted.

Surgical anatomy of the frontonasal area is reviewed and certain variations and landmarks are stressed

Physiologic principles related to frontal sinus surgery are discussed

Thirty-one patients with frontal sinusitis operated upon over a period of 20 years are reviewed The following pertinent observations are noted

1 Etiologic factors of significance are associated maxillary and ethmoid sinusitis and frontal sinus trauma

2 Radiologic interpretation of activity of disease is difficult with conventional views, but polytomography often reveals specific changes.

3 Staphylococcus aureus and Diplococcus pneumoniae are the most frequent pathogens cultured.

4 Pathologic findings often demonstrated are irreversible mucosal disease and bone absorption

5 Surgical procedures of incision, drainage and trephine lead to a high recurrence rate

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A Review

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UPPSALA 1970

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Preface

One cannot usually foretell from what aspect a biological enigma should be attacked to lead in the most direct fashion to a solution. Otosclerosis is at present a biological enigma. Facts about otosclerosis may be gathered by several means and may be considered in several ways and in the light of different disciplines. The future alone will tell us whether any of the facts and reasoning currently available are the keys to the problem At present we cannot foretell (H M Frost, M.D 1962).

The variety and volume of experimental data on otosclerosis which have accumulated during the past decade as well as their increasingly rapid appearance make attempts at evaluating the *status quo* of research in this field exceedingly difficult. It is our opinion that a comprehensive review of the subject with emphasis on recent biochemical contributions would be a valuable addition to the literature An attempt at such a review is presented below

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Preface

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Histopathology

Otosclerosis is a disease of the bony labyrinthine capsule, often developing in areas in which embryonic cartilage persists. Viewed under the light microscope, the pathological process is characterized by resorption of normal bone often around blood vessels and its replacement with cellular fibrous connective tissue. Areas undergoing active resorption contain numerous osteoclasts and are extensively vascularized. Within the matrix of the invading connective tissue reticular cells and fibroblasts assume the character and activity of osteoblasts and later osteocytes. Calcium is deposited irregularly in the matrix, resulting in the formation of an immature weblike bone. This bone contains a large amount of ground substance with few collagen fibers, hence its blue color (basophilia) when stained with hematoxylin and eosin. The immature bone is eventually resorbed and replaced by a different type of weblike bone containing little ground substance and large numbers of collagen fibers. This is acidophilic and stains red with hematoxylin and eosin. Finally true lamellar bone may be laid down within the weblike bone with the result that the otosclerotic focus assumes a mosaic like appearance. The process of resorption and re placement continues irregularly both within the focal area and at its margin. Microfoci, demonstrable only with the electron microscope, occur in the vicinity of the larger more evident foci and the lesion appears to enlarge by fusion of these microfoci (Chevance et al., 1969). Under the light microscope extension of the disease manifests itself as a network of trabeculae.

Otosclerotic foci may remain active or become quiescent. Active lesions are characterized microscopically by the spongy appearance of the bone, by the presence of large numbers of cells, especially osteoclasts, and by extensive vascularization. Inactive otosclerotic lesions exhibit a more compact bone, are poorly vascularized, and contain few cells. Foci within the same temporal bone may be in the same or dif ferent stages of activity. A single lesion may contain both active and quiescent regions. Finally as the disease progresses, a focus may exhibit alternating periods of activity and quiescence as it proceeds to its inactive terminal stage.

Occurrence of Otosclerotic Foci Areas of Predilection

An otosclerotic lesion may occur in any region of the bony labyrinthine capsule. Only rarely is it located external to this area in which case it may appear in the carotid canal, tegmen, cochleariform process, or incudo-stapedial or incudo-malleolar joints (Nager 1969). Most frequently (80 to 90 percent of all cases) the primary lesion is found in the region anterior to the oval window (Guild, 1944 Nylén, 1949 Fleischer 1958 Beickert, 1963). Despite the high incidence of foci in this area, in only approximately 10 percent of these cases does the disease invade the annular ligament and spread to the stapedial footplate causing ankylosis. The latter manifests itself clinically as the conductive deafness characteristic of otosclerosis. Isolated primary otosclerosis of the footplate is rare, observed in only 12 per cent of the cases studied by Guild (1944) and in 5 percent of the cases studied by Rüedi &



Fig 2 *A* external auditory canal; *B* malleus and tympanic membrane *C* incus; *D* stapes, *E* otosclerotic foci *F* vestibule; *G* facial nerve; *H* semicircular canals, *I* cochlea *J* tympanic cavity *K*, eustachian tube *L*, internal auditory canal.

causes ankylosis of the stapes resulting in a conductive deafness. Since the latter complicates only approximately 10 percent of all cases of otosclerosis, histological examination of the otic capsule is necessary in order to ascertain the true incidence of the disease, hence the term "histological otosclerosis Therefore, studies giving statistics of the incidence of clinical otosclerosis are descriptive only of the incidence of stapedial ankylosis. Studies giving data describing the distribution of "histological" otosclerosis, however are surveys of the total incidence of the disease regardless of whether or not it is clinically manifest.

Information concerning the ratio of distribution of otosclerosis between the sexes derives from both clinical and histological investigations Numerous authors have reported the incidence of stapedial ankylosis in females to be twice that in males (Bauer & Stein, 1925 Davenport et al 1933 Schmidt, 1933 Gray 1934 Nager 1939 Cawthorne, 1955 Shambaugh, 1956 Wolff, 1958 Larsson, 1960 Hlavecek & Chladek, 1963 Altmann et al., 1967) Our own analysis of 2 600 operative cases of otosclerosis yields a sex ratio of 1 6 females to 1 0 males (Soder et al., unpublished data) However histological studies have shown the incidence of otosclerosis to be approximately equal in males and females (Weber 1935 Engström, 1940 Guild, 1944 Altmann et al., 1967). Analysis of data combined from a number of the larger studies shows the incidence of histological otosclerosis to be 51.5 percent in males and 48.5 percent in females, giving a ratio of 1.00 males to 0 94 females. The incidence of stapedial ankylosis is reported to be 38.2 percent in males and 61 8 percent in females, a ratio of 1 61 females to 1.00 males (Altmann et al., 1967).

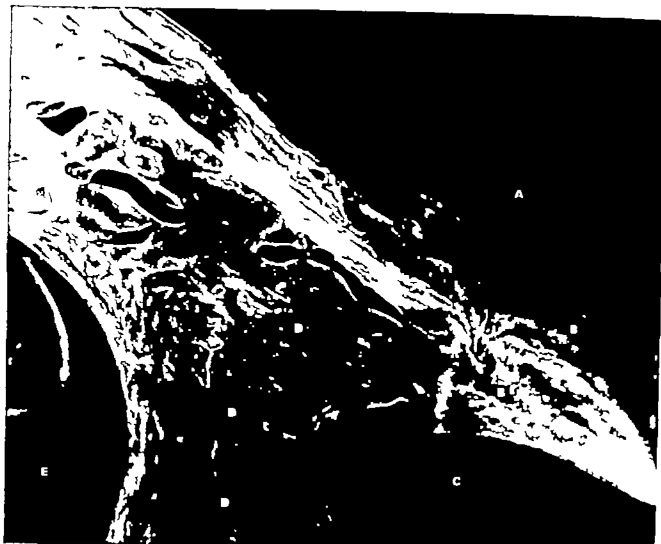


Fig 1 *A* tympanic cavity *B* otosclerosis in foot plate *C* vestibule *D* otosclerotic foci *E* cochlea.

Spöndlin (1957) Another region frequently affected (often simultaneously with that of the oval window) is the area of the round window The latter is involved in 30 to 40 percent of all cases (Guild 1944 Nylén 1949 Fleischer 1958 Rüedi & Spöndlin 1957) Less often otosclerotic foci occur in other areas of the capsule, e.g. in the cochlear and semi-circular canal regions and/or at the anterior circumference of the internal auditory meatus

Although otosclerosis is usually focal (90 percent of all cases) it can develop as a diffuse process involving large areas of the otic capsule. The diffuse variety normally results from confluence of the focal areas, but primary diffuse otosclerosis does occur

In most cases otosclerosis affects both temporal bones unilateral otosclerosis occurring in only 25 percent of all cases (Guild 1944 Nylén, 1949 Fleischer 1958)

Incidence of Otosclerosis Sex Ratio and Demographic Distribution

In any assessment of the ratio of distribution of otosclerosis between the sexes or of the incidence of the disease in various populations, one must appreciate the distinction between clinical and "histological" otosclerosis. The disease can be detected *clinically only if it*



Fig. 2 *A* external auditory canal, *B* malleus and tympanic membrane *C* incus, *D* stapes, *E* otosclerotic foci, *F* vestibule *G* facial nerve *H* semicircular canals; *I* cochlea *J* tympanic cavity *K* eustachian tube *L* internal auditory canal.

causes ankylosis of the stapes resulting in a conductive deafness. Since the latter complicates only approximately 10 percent of all cases of otosclerosis, histological examination of the otic capsule is necessary in order to ascertain the true incidence of the disease, hence the term "histological otosclerosis" Therefore, studies giving statistics of the incidence of clinical otosclerosis are descriptive only of the incidence of stapedial ankylosis. Studies giving data describing the distribution of histological otosclerosis, however are surveys of the total incidence of the disease, regardless of whether or not it is clinically manifest

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Both clinical and histological studies of incidence have limitations, to a greater or lesser degree, which must be appreciated when evaluating their validity Although figures pertaining to clinical otosclerosis are computed from a large number of cases and thus are statistically significant, the cases included are not entirely unselected to the extent that patients are by definition unrepresentative of the entire population In fact, the higher incidence of clinical otosclersosis in females may be a reflection of a "natural selectivity" among the patients themselves i e it may be due to a greater willingness of females to consult a physician about hearing impairment.

The results of the histological studies of the incidence of the disease are even more difficult to evaluate than are those of the clinical studies In addition to suffering from selectivity the data are not statistically significant because of the small number of temporal bones available for examination In fact, the number of temporal bones which would be required in order to obtain significant data is impracticably large The largest series analysed to date (Guild 1944) includes 974 temporal bones of which only 47 were found to exhibit otosclerosis

It is clear that a method other than histological examination of temporal bones is essential in order to obtain significant data of the total incidence of the disease The comparatively recent technique of polytome laminography would seem to be the most promising alternative (Derlacki & Valvassori 1965) The advantages of this technique are that otosclerotic lesions can be detected in the living patient and that the locations and extent of the lesions throughout the otic capsule can be visualized The problem of non-random selection of persons would remain but it is likely that with the extremely large numbers of persons who can easily be examined by this method, collection of valid data is at least feasible

The available data on the frequency of occurrence of otosclerosis in various populations suffer from the same limitations as those pertaining to the sex ratio They are not statistically significant, either because the cases studied were not entirely unselected or because they were too few in number However some assessment of the distribution of the disease can be derived from them if the restrictions on their validity are kept in mind A compilation of figures from the studies of Engström (1940) and Guild (1944) indicates that among 601 white American adults, the incidence of otosclerosis is 8 3 percent while the incidence of stapedial ankylosis is only 0 99 percent (Altmann et al 1967) That is, although every tenth white adult has otosclerosis, hearing difficulties affect only every one hundredth individual Information on the incidence of the disease in populations other than those of white American adults is limited A study of temporal bones of adult American Negroes indicated that otosclerosis is seven times less frequent than in the adult white population (Altmann et al 1967) The few existing investigations of otosclerosis in African Negroes (Van Fick, 1964) and in American Indians (Gregg et al 1965) suggested that the disease is almost non-existent" in the populations studied Otosclerosis also appears to be extremely rare in Japanese (Horiguchi 1953 Takahara et al., 1959) Chinese (Altmann et al., 1967) and Indonesian (Nizar 1960) populations However the incidence of stapedial ankylosis in populations of both Northern and Southern India is high 20 to 30 percent as compared with 10 percent in white American populations (Sinha 1963 Kapur & Patt, 1966) These limited data suggest that otosclerosis is of relatively frequent occurrence only in white American and in Indian populations.

Etiology of Otosclerosis
The Genetic Basis

The familial pattern of otosclerotic deafness observed stimulated investigations which proved the disease to be heritable. A clinical study of 257 families with otosclerosis demonstrated the mode of inheritance to be a simple autosomal dominance with a penetrance of the abnormal gene of 25 ± 8.5 percent (Larsson, 1960). A survey by Morrison (1967) of 146 otosclerotic patients and their families corroborated the pattern of inheritance but established penetrance at 40 percent.

It is interesting that "isolated" instances of otosclerosis in the offspring of matings between apparently normal parents accounted for 43 cases, or 30 percent of all cases included in Morrison's study. With a penetrance of only 40 percent, most of these cases can be explained by assuming that the abnormal gene is present in the parents' genotype but fails to manifest itself phenotypically. New autosomal dominant mutations can account for only a small percentage of the isolated cases. Morrison calculates that 1.4 percent of the abnormal alleles are dropped per generation and that the theoretical mutation rate is of the order of 49 10. Thus, only two out of 43 (4.7 percent) of these cases are theoretically likely to be due to new mutations. Since, however, the isolated cases are statistically more frequent among secondary births, it is probable that at least some are due to new mutant alleles. A few cases might result from an alternate mode of inheritance, e.g., homozygous autosomal recessivity. Indeed, the phenomenon of similar phenotypes resulting from different genotypes does occur in man. Finally, some cases may be caused not by otosclerosis but rather by other diseases producing a conductive deafness mimicking that of otosclerosis. This possibility cannot be ruled out in a purely clinical study.

Since otosclerosis is not a sex-linked character one would expect a sex ratio incidence of 1:1. As mentioned above, histological studies of temporal bones have confirmed that this ratio prevails. Observations from purely clinical studies indicate that otosclerosis occurs twice as frequently in females as in males, possibly for the behavioral reason mentioned previously. However, Morrison's random sampling of 613 individuals, from which he obtained the 146 otosclerotics included in his study, yielded the following results. Of 338 females, 137 (40.5 percent) had otosclerosis; of 275 males, 88 (32 percent) were otosclerotic. In this case, the sex ratio from a clinical study is near unity.

The possibility of a linkage between otosclerosis and characters for which the genetics are well-established has been investigated, as has the occurrence of abnormal karyotypes. Jannvzzis (1929) investigated five families with otosclerosis and observed a linkage between otosclerosis and the ABO blood group system. However, the validity of the results in Jannvzzis' study is questionable because of incomplete genotyping and the probability that the observed deafness was actually caused by otosclerosis in only two of the five families. In a study of over one hundred otosclerotics, Morrison (1967) found no evidence of any association of otosclerosis with a particular genotype in the ABO, MN, or Rhesus blood groups, the secretor states, or with a specific or abnormal haptoglobin genotype. With respect to the latter, we have also reported a normal distribution of serum haptoglobin among otosclerotics (Sofer et al., 1963). An association of otosclerosis with the ability to taste phenylthiocarbamide is statistically significant (Morrison, 1967), indicating that alleles for the two characters are located quite close to each other on the same chromosome. Tato and co-workers (1963) reported the presence of chromosome ab-

Both clinical and histological studies of incidence have limitations, to a greater or lesser degree, which must be appreciated when evaluating their validity Although figures pertaining to clinical otosclerosis are computed from a large number of cases and thus are statistically significant, the cases included are not entirely unselected to the extent that patients are by definition unrepresentative of the entire population In fact, the higher incidence of clinical otosclerosis in females may be a reflection of a "natural selectivity" among the patients themselves i e it may be due to a greater willingness of females to consult a physician about hearing impairment.

The results of the histological studies of the incidence of the disease are even more difficult to evaluate than are those of the clinical studies In addition to suffering from selectivity the data are not statistically significant because of the small number of temporal bones available for examination. In fact, the number of temporal bones which would be required in order to obtain significant data is impracticably large The largest series analysed to date (Guild, 1944) includes 974 temporal bones of which only 47 were found to exhibit otosclerosis

It is clear that a method other than histological examination of temporal bones is essential in order to obtain significant data of the total incidence of the disease The comparatively recent technique of polytome laminography would seem to be the most promising alternative (Derlacki & Valvassori 1965) The advantages of this technique are that otosclerotic lesions can be detected in the living patient and that the locations and extent of the lesions throughout the otic capsule can be visualized. The problem of non-random selection of persons would remain but it is likely that with the extremely large numbers of persons who can easily be examined by this method, collection of valid data is at least feasible

The available data on the frequency of occurrence of otosclerosis in various populations suffer from the same limitations as those pertaining to the sex ratio They are not statistically significant, either because the cases studied were not entirely unselected or because they were too few in number However some assessment of the distribution of the disease can be derived from them if the restrictions on their validity are kept in mind A compilation of figures from the studies of Engström (1940) and Guild (1944) indicates that among 601 white American adults, the incidence of otosclerosis is 8 3 percent while the incidence of stapedial ankylosis is only 0 99 percent (Altmann et al 1967) That is, although every tenth white adult has otosclerosis, hearing difficulties affect only every one hundredth individual Information on the incidence of the disease in populations other than those of white American adults is limited. A study of temporal bones of adult American Negroes indicated that otosclerosis is seven times less frequent than in the adult white population (Altmann et al., 1967) The few existing investigations of otosclerosis in African Negroes (Van Fick 1964) and in American Indians (Gregg et al. 1965) suggested that the disease is almost non-existent" in the populations studied Otosclerosis also appears to be extremely rare in Japanese (Horiguchi, 1953 Takahara et al 1959) Chinese (Altmann et al 1967), and Indonesian (Nizar 1960) populations However the incidence of stapedial ankylosis in populations of both Northern and Southern India is high 20 to 30 percent as compared with 10 percent in white American populations (Sinha 1963 Kapur & Patt, 1966) These limited data suggest that otosclerosis is of relatively frequent occurrence only in white American and in Indian populations.

Etiology of Otosclerosis
The Genetic Basis

The familial pattern of otosclerotic deafness observed stimulated investigations which proved the disease to be heritable. A clinical study of 257 families with otosclerosis demonstrated the mode of inheritance to be a simple autosomal dominance with a penetrance of the abnormal gene of 25 ± 8.5 percent (Larsson, 1960) A survey by Morrison (1967) of 146 otosclerotic patients and their families corroborated the pattern of inheritance but established penetrance at 40 percent.

It is interesting that "isolated" instances of otosclerosis in the offspring of matings between apparently normal parents accounted for 43 cases, or 30 percent of all cases included in Morrison's study With a penetrance of only 40 percent, most of these cases can be explained by assuming that the abnormal gene is present in the parents genotype but fails to manifest itself phenotypically New autosomal dominant mutations can account for only a small percentage of the isolated cases. Morrison calculates that 1 4 percent of the abnormal alleles are dropped per generation and that the theoretical mutation rate is of the order of 49 10^{-6} Thus, only two out of 43 (4 7 percent) of these cases are theoretically likely to be due to new mutations Since however the isolated cases are statistically more frequent among secondary births, it is probable that at least some are due to new mutant alleles. A few cases might result from an alternate mode of inheritance e.g. homozygous autosomal recessivity Indeed, the phenomenon of similar phenotypes resulting from different genotypes does occur in man. Finally some cases may be caused not by otosclerosis but rather by other diseases producing a conductive deafness mimicking that of otosclerosis This possibility cannot be ruled out in a purely clinical study

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normalities in otosclerosis, i.e trisomy and tetrasomy in patients aged 13 to 15 years However in chromosome studies of nine cases of otosclerosis and three cases of osteogenesis imperfecta, Morrison (1967) found no abnormal karyotypes More extensive studies are necessary to resolve this conflict

The association of (conductive) deafness with osteogenesis imperfecta and blue sclerae has been documented by authors since the syndrome was originally described by van der Hoeve and de Kleyn. Wullstein and co-workers (1960) and Ogilvie & Hall (1962) argued from results of histological studies that otosclerosis is a local manifestation of osteogenesis imperfecta, indicating that both are determined by the same abnormal allele It is true that a large number of children affected with osteogenesis (with or without blue sclerae) who survive to adult life develop deafness which follows a clinical pattern similar to that of otosclerosis In Smårs (1961) study of individuals with osteogenesis imperfecta, 22.6 percent have some degree of deafness, the age-of-onset pattern mimicking *that of otosclerosis. As in the otosclerosis, the* severity of the deafness is osteogenesis was enhanced by pregnancy and varied among families, the most serious cases beginning in adolescence and progressing rapidly

Despite such similarities, the numerous genetic, histological and biochemical factors which differ between otosclerosis and osteogenesis imperfecta suggest that the theory of a common abnormal gene is untenable Otosclerosis occurs only in man, whereas osteogenesis has been demonstrated in other animals (Ogilvie & Hall 1962) Isolated" cases are frequent in otosclerosis (30 percent) rarer in osteogenesis (approximately 9 percent) Blue sclerae are associated with otosclerosis in less than 0.5 percent of all cases, while 85 percent of all individuals with osteogenesis have blue sclerae Deafness in otosclerosis is severe and sensorineural in less than 10 percent of all cases in osteogenesis severe sensorineural hearing loss is much more frequent, occurring in 40 percent of all cases Secondary manifestations of osteogenesis imperfecta are widespread (bones, joints, sclerae teeth, blood vessels) no skeletal abnormalities or hemorrhages were found associated with otosclerosis in Morrison's study Where otosclerosis and osteogenesis imperfecta co-exist, the two may be clearly distinguished histologically (Altmann & Kornfeld, 1967 Bretlau & Balslev Jørgensen, 1969) osteoclasts are absent and fibroblasts infrequent in osteogenesis while both are common in otosclerosis (Chevance, 1965 Clerc & Chevance, 1965) Free sulfhydryl groups were detected biochemically in otosclerotic foci but not in osteogenic bone (Chevance, 1965) Finally otosclerosis is a common disease, osteogenesis is rare.

It may b concluded that there is no good evidence in support of the hypothesis that the two conditions result from the same abnormal gene. *The evidence is good, however* that they belong to the same family of diseases, the inherited collagen abnormalities All of the latter have an autosomal dominant mode of inheritance with incomplete penetrance of the abnormal gene Phenotypically the expression varies that is, there are degrees of clinical severity In all of these diseases the defect probably affects the same enzyme system, that concerned with the production and turnover of collagen. Deafness is osteogenesis is described by Morrison (1967) as a phenocopy" *of otosclerosis Additional* "phenocopies" of otosclerosis may include Paget's disease (osteitis deformans) congenital absence of the stapes, rheumatoid arthritis (with involvement of ossicular joints) *Von* Recklinghausen's disease (osteitis fibrosa cystica), and chronic adhesive otitis.

Basic Research on Pathogenesis
The Biochemical Data

Until recently the major contribution to expansion of knowledge of the pathogenesis of otosclerosis derived from histological and histochemical data. Histological studies have been invaluable in defining the morphological changes characterizing the disease process and in describing the microscopic appearance of the lesion. Histochemical studies have shown that otosclerotic foci are metabolically active, particularly during the stages of growth and invasion. However the procedures employed in histochemistry have inherent technical difficulties which restrict the amount and type of information which can be extracted from them. Identification and quantitative measurement of small molecular imbalances and highly specific chemical reactions require the more sensitive techniques of biochemical analysis. Ultimately histological and histochemical descriptions of morphological events must be correlated with biochemical information in order to construct a complete and accurate picture of the otosclerotic process.

Biochemical data on otosclerosis are not abundant. However since Maurer's initial study in 1961 information has been forthcoming at an increasing rate. To date, biochemical studies of otosclerosis have focused on four major tissue constituents: enzymes, components of the bone matrix, hormones, and inorganic constituents of bone.

ENZYMES

Since otosclerosis is a genetically-determined disease, it is likely that the initial biochemical manifestation is either a defective control of the synthesis of an enzyme(s) or the production of a completely or partially non-functional enzyme(s). The biochemical search for aberrant enzyme behaviour was given an impetus by significant histochemical findings. Albernaz & Covell (1961) found large amounts of succinate dehydrogenase and cytochrome oxidase in osteoclasts, fibroblasts, blood vessel walls (and smaller amounts in osteocytes) of otosclerotic foci when compared with control stapedes, suggesting that the former have a high level of respiratory activity. Large concentrations of acid phosphatase have been demonstrated in osteoclasts and in the matrix of otosclerotic bone (Albernaz & Covell, 1961). Alkaline phosphatase has been detected both in the cells (osteoblasts, osteoclasts, fibroblasts) and in the otosclerotic matrix (Ricci, 1962; Arslan & Ricci, 1963). Leucine aminopeptidase (Alberti & Tarkannen, 1963) and the non-specific esterase complex (Ardouini & Wegmann, 1961; Chevance, Clerc & Bouche, 1962, Alberti & Tarkannen, 1963) have been found in blood vessel walls, perivascular fibroblasts, and particularly in osteocytes close to blood vessels in the otosclerotic focus. Cabrini (1961) however found leucine aminopeptidase activity in the focus to be completely extracellular.

Despite their desirability comparative biochemical studies of enzyme activity in otosclerotic and normal bone are relatively few. Maurer's pioneer study (1961/62) indicated that there is an increase in the total nitrogen content and a decrease in alkaline phosphatase activity in endochondral bone (ossicles, semicircular canal, promontory) from otosclerotics. Maurer concluded that these results were inexplicable on the assumption of an increase in the number or activity of cellular elements (metabolically active) but rather derived from a numerical increase in the fibrils (metabolically inactive). We have carried out comparative studies of extractable protein and certain enzymes (lactate dehydrogenase, malate dehydrogenase, amino aspartic transferase, al-

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dolase glucose-6-phosphate dehydrogenase acid and alkaline phosphatases) in mallei incudes, stapedes (endochondral bone) and in cortical (lamellar) bone from otosclerosis and non-otosclerotic patients (Soifer et al 1967 *a b* 1969 *a*) Extractable protein is increased in mallei and incudes and decreased in cortical bone from otosclerotics as compared to normal, while the protein content of stapedes is comparable in otosclerotic and non-otosclerotic patients Determination of enzyme activities indicate that the overall level of metabolic activity (as measured by the above mentioned enzymes) of both normal and otosclerotic stapedes although not the same, is considerably higher than the metabolic activity of mallei incudes, and cortical bone One can speculate that this inherently high metabolic rate may be one factor which gives the stapedes their predisposition to the development of foci

Among the enzymes investigated however only two lactate dehydrogenase and alkaline phosphatase, show statistically significant differences in activity between otosclerotics and non-otosclerotics In all the samples of bones studied, the activity of lactate dehydrogenase is significantly lowered when otosclerosis is present Lactate dehydrogenase is 49 percent lower in stapedes, 26 percent lower in cortical bone, and 15 percent lower in mallei and incudes obtained from otosclerotic patients. A particularly striking increase in alkaline phosphatase activity is found in involved stapedes (Soifer et al 1969 *a*) The average activity in otosclerotic is approximately eight times that in normal stapedes

Since in whole stapedes the dilution effect of the crura, which usually do not contain foci, is to effectively reduce the magnitude of the observed increase in alkaline phosphatase, we measured the activity of the enzyme in single footplates which were moderately or heavily involved as assessed microscopically The results appear in Table I

The values obtained for normal footplates were comparable to those obtained previously for normal whole stapedes (Soifer et al., 1969 *a*) Values for involved stapedes were either comparable to or greater than those obtained previously This would be expected by virtue of elimination of the dilution effect of the crura. These data confirm that there is an increase in alkaline phosphatase activity in otosclerotic bone. There appears to be no consistent correlation between the amount of otosclerotic growth and the level of enzyme activity However since the footplates were not examined histologically prior to biochemical assay it cannot be assumed that all of the foci present were active Inactive foci would add to the total amount of otosclerotic growth, but they could also dilute" the enzyme activity as do the crura

The fact that we have observed no change in the concentration of protein but have found a considerable elevation of the alkaline phosphatase activity in involved stapedes suggests that there may be an increase in the cellular metabolic activity of this ossicle in otosclerosis. This conflicts with Maurer s suggestion of a numerical increase in non-metabolic constituents (collagen fibrils) based on his observation of an increased nitrogen content in otosclerotic stapedes However the fact that in otosclerosis changes (page 14) whatever their nature, are observed in tissues other than those having otosclerotic foci indicates that the biochemical effects of the disease are generalized that is they are not confined to focal areas.

Table I *Alkaline phosphatase activity in stapedial footplates*

Stapedial footplates	Degree of Oto-sclerosis	Alkaline phosphatase activity (× 10⁻⁴ μ moles min/mg tissue)
1 Otosclerotic	Moderate	13.[illegible]
2. Otosclerotic	Moderate	37 4
3. Otosclerotic	Heavy	11 6
4 Otosclerotic	Heavy	110.6
5 Normal (labyrinthectomy)	—	3.1
6. Normal (autopsy)	—	6.1
7 Normal (autopsy)	—	1 2
8 Normal (autopsy)	—	3.7

Protein and enzymes in body fluids and in tissues other than bone have been investigated in an effort to measure the extent of such generalized changes Protein in vein tissue from otosclerotics is lower than normal while lactate dehydrogenase activity is elevated 30 percent above normal (Solfer et al., 1965 *a* *b*) Normal levels of protein (Naumann, 1964) and alkaline phosphatase activity (Fowler 1948 Riskaer 1949 Sofer et al., 1965 *a*) are found in sera from otosclerotics and the serum isoenzyme pattern of alkaline phosphatase shows no abnormal qualitative alterations (Sofer et al., 1963). Other tissues and additional enzymes must be examined in order to assess the total extent of generalized alterations.

THE BONE MATRIX

In addition to the enzymatic changes, the possibility of alterations in the matrix of otosclerotic bone has been investigated. The histochemical evidence indicates that ground substance is active, with large amounts of acid mucopolysaccharide observed in the otosclerotic foci (Albernaz & Covell, 1961). Yet the ground substance of otosclerotic bone appears to be no more or no less active than that of other newly-formed bone (Albernaz & Covell, 1961 Chevance, Clere & Bouche, 1962) The PAS-positive material does vary in density however in different parts of the otosclerotic lesion. This suggests a compositional change, possibly an alteration in the degree of polymerization of the intercellular substance Perhaps the latter is in a more condensed state and less dynamic.

As mentioned above, the results of Maurer's biochemical study (1961 62) indicate an increase in the fibrillar content of otosclerotic bone Yet, under the polarizing microscope the collagenous matrix of the focus (irregularly arranged fibrils) is similar to that of other newly formed fibrous bone (Cabrini, 1961 Alberti & Tarkannen, 1963) but different from that of normal endochondral bone (the fibrils are arranged in a more orderly pattern) This suggests that otosclerotic changes in the fibrils, as well as in the ground substance, may be organizational rather than absolute. The cells of the focus may be abnormally immature so that only eventually and slowly is the immature matrix remodeled into typical lamellar haversian bone (Cabrini, 1961). The demonstration of leucine aminopeptidase activity in the newly-formed ground substance theoretically supports this idea, as it is postulated that the presence of this enzyme is indicative of immature fibrous tissue, especially immature fibroblasts, and may function in the formation of collagen fibrils. With the electron microscope, interwoven collagenous bundles are seen intricately arranged but here the collagen matrix of the otosclerotic focus appears denser than that of normal fibrous bone (Chevance et al., 1969) This would appear to support Maurer's postulated numerical increase in fibrils.

In our investigation of the matrix of otosclerotic bone, we measured hexosamine, and hydroxyproline and proline (indices of total mucopolysaccharide and total collagen, respectively) in ossicles and samples of bone from other regions of the otic capsule and found no abnormal changes in tissue from otosclerotics (Solfer et al., 1969 *d*) There are inherent regional differences in the hexosamine content of the otic capsule bone e.g., the highest amount is found in stapedial footplates, followed by crura, promontory semicircular canal capsule, round and oval window mallei, heads of mallei, incudes, and cortical bone, in that order But we found no correlation between the regional variations and the frequency of occurrence of otosclerotic foci. Although the total mucopolysaccharide in otosclerosis does not appear to be altered, it is conceivable that differences may occur in the proportions of the specific types of mucopolysaccharide molecules (the relative amounts of acid, neutral, sulfated, and non-sulfated mucopolysaccharides may change) as well as in the degree of their polymerization. The histochemical finding of increased acid mucopolysaccharide in active foci may also be valid biochemically This, of course would presuppose a decrease in neutral

mucopolysaccharide in order that the total remain unchanged

The constancy of the ratio of hydroxyproline to proline in all samples investigated suggests that intermolecular differences in the fibrillar content do not occur as a result of otosclerosis (Soifer et al 1969 *d*) However this does not rule out differences in fibrillar organization which may well exist. The question of whether there is or is not a numerical increase in collagen fibrils in otosclerosis remains at present, unresolved

Efforts have been made to determine if changes attributed to otosclerosis occur in the matrices of tissues other than bone and, in the event that such changes do occur if they are reflected in urinary excretory products An increase in the amount of ground substance in the corium of the skin as well as a decrease in the number of fine collagen fibers and an increase in the number of elastic fibers is reported by Vyslonzil (1965) Bentzen (1961) and Stadil (1961) However biochemical analysis of the total mucopolysaccharide and total acid mucopolysaccharide fractions of vein revealed no differences between otosclerotics and non otosclerotics (Soifer et al 1969 *d*) Thus far the number of studies devoted to investigating generalized changes is too small to provide a basis of valid assessment However indications are that if such generalized changes do occur they are not reflected in the products of urinary excretion of amino acids (and by inference collagen) and hexosamine in otosclerotic patients and found no variations from normal Similarly we found urinary acid mucopolysaccharide excretion to be the same in otosclerotics and non-otosclerotics (Soifer et al 1969 *e*) In addition, electrophoretic separation showed a similar migratory distribution of urinary mucopolysaccharides

HORMONES

The dynamic processes of bone turnover affect both mineral and organic constituents Normally collagen is only slightly subject to turnover It must, however be replaced after resorption such as occurs in otosclerosis. It is currently theorized that physiological replacement and resorption are under hormonal control, specifically that the sex hormones, androgens and estrogens provide the stimulus for replacement while the adrenocortical hormones activate resorption (McLean & Urist, 1961) Under normal physiological conditions there exists a balance between resorption and replacement of the matrix If this view is accepted, it follows that the pathological resorption and replacement processes of otosclerosis might reflect a hormonal imbalance.

Certain clinical observations of the pathogenesis and progress of otosclerosis are indicative of the involvement of hormones The onset of otosclerotic deafness frequently coincides with puberty and the incidence of onset increases with age (Wullstein, 1960 Larsson, 1960) Since however the disease is histologically detectable long before it is clinically manifest (Larsson, 1960) the implication is that hormones may in some way enhance the progress of the disease. This is supported by the observation that otosclerotic deafness seems more severe during pregnancy It is, of course, possible that this enhancement effect is only apparent since the patient normally has a heightened consciousness of body functions during this period

The principal experimental approach toward ascertaining the significance of hormones in the pathogenesis of otosclerosis has been the measurement of levels of urinary steroids However studies of this type are few in number and results do not always agree. Herrmann & Maurer (1955) reported decreased levels of urinary androgens in otosclerotic patients, while Vyslonzil & Klein (1961) found these levels to be normal An increase in the level of urinary estrogens in otosclerotic patients particularly in males aged 20 to 50 years, has been reported (Vyslonzil & Klein, 1961 Vyslonzil 1963) More recently however DeJorge and co-workers (1965) found normal levels of estrogens in otosclerotics (both males and females) Changes" in the amounts of 17 ketosteroids

in otosclerotic patients were reported by Maggio (1953) and by Herrmann & Maurer (1955) But Vyslonzil & Klein (1961) found nine out of fourteen male otosclerotic patients to have 17-ketosteroid levels in the normal range. This result is substantiated by our more extensive studies (Soifer et al 1969 f in preparation) which also shows the excretion of 17-hydroxy-steroids to be normal in otosclerotics.

The conflicting results issuing from the various studies preclude, at present, even a hypothetical evaluation of the specific function (s) of hormones in the pathogenesis of otosclerosis. That hormones are involved appears certain merely by virtue of their ubiquitous influence on physiological processes in general and the clinically-observed enhancement of otosclerosis by puberty and pregnancy Otosclerosis does result from an upset in the normal dynamic equilibrium between resorption and accretion of bone However it is also true that accretion in otosclerosis consists in deposition of pathological fibrous bone and thus cannot merely result from an upset in normal physiological activity Therefore, a simple change in the relative levels of the sex and adrenocortical hormones, if these do indeed control resorption and accretion, cannot alone account for the pathogenic process but rather may be one of several contributing factors.

INORGANIC CONSTITUENTS

Because of the fundamental relationship of minerals and ions to bone, investigations have been directed toward determining if pathological changes in the inorganic constituents of the matrix occur as a result of otosclerosis. If only because otosclerotic bone resembles immature fibrous bone, one would expect incomplete mineralization (Frost, 1962) The radiological picture of cochlear foci supports this hypothesis (Derlacki & Valvassori, 1965). Recently the total mineral content of one malleus and several incudes obtained from otosclerotics was investigated by a technique based on measurement of bone density i.e. monoenergetic photon beam transmission (Evens & Henkin, 1969) As the authors indicate, evaluation of the findings is severely restricted by the lack of a sufficient number of samples, among other things. But the limited data are indicative of a lower than normal mean mineral content in mallei and incudes from otosclerotics. If further studies confirm this tentative result, alterations in the mineral content of the matrix of uninvolved bone could be included among the "generalized changes" caused by otosclerosis.

In addition to studies of total mineral content, individual elements and ions have been investigated in bone and serum from otosclerotics. The results of several studies appear in Table II It is evident that agreement among studies is the exception. Methodology appears to be a significant factor in the conflict. For example, Maurer's biochemical technique demonstrated a lower than normal calcium and phosphorus content in stapedes from otosclerotics while the neutron activation analysis that we used yielded values comparable to those for normal stapedes. The conflicting results give rise to alternate interpretations of the state of mineralization of otosclerotic bone. Maurer's results indicate that mineralization is incomplete and, coupled with data pointing to an increased fibrillar content, suggest that an altered apatite fibril relationship characterizes otosclerotic bone. Our results do not deny the existence of such compositional change but suggest that it may consist purely of differences in the structural relationship among the components of the matrix rather than of absolute changes in the total amount of individual minerals or of fibrils. Further analyses will perhaps resolve the conflict. However it cannot be denied that the ultrasensitivity of neutron activation analysis (quantities can be detected in a range of 0 1 to 100 µg per sample) coupled with the requirement for minimal amounts of tissue (fractions of milligrams) make it a most valuable and accurate method for quantitative measurement of minerals and other elements in bone.

At best, quantitative measurement of elements in otosclerotic bone indirectly reflect a momen-

mucopolysaccharide in order that the total remain unchanged.

The constancy of the ratio of hydroxyproline to proline in all samples investigated suggests that intermolecular differences in the fibrillar content do not occur as a result of otosclerosis (Soifer et al 1969 *d*) However this does not rule out differences in fibrillar organization which may well exist. The question of whether there is or is not a numerical increase in collagen fibrils in otosclerosis remains at present, unresolved

Efforts have been made to determine if changes attributed to otosclerosis occur in the matrices of tissues other than bone and in the event that such changes do occur if they are reflected in urinary excretory products An increase in the amount of ground substance in the corium of the skin as well as a decrease in the number of fine collagen fibers and an increase in the number of elastic fibers is reported by Vyslonzil (1965) Bentzen (1961) and Stadil (1961) However biochemical analysis of the total mucopolysaccharide and total acid mucopolysaccharide fractions of vein revealed no differences between otosclerotics and non-otosclerotics (Soifer et al 1969 *d*) Thus far the number of studies devoted to investigating generalized changes is too small to provide a basis of valid assessment. However indications are that if such generalized changes do occur they are not reflected in the products of urinary excretion of amino acids (and by inference collagen) and hexosamine in otosclerotic patients and found no variations from normal. Similarly we found urinary acid mucopolysaccharide excretion to be the same in otosclerotics and non-otosclerotics (Soifer et al 1969 *e*) In addition, electrophoretic separation showed a similar migratory distribution of urinary mucopolysaccharides.

HORMONES

The dynamic processes of bone turnover affect both mineral and organic constituents Normally collagen is only slightly subject to turnover It must, however be replaced after resorption such as occurs in otosclerosis. It is currently theorized that physiological replacement and resorption are under hormonal control specifically that the sex hormones, androgens and estrogens, provide the stimulus for replacement while the adrenocortical hormones activate resorption (McLean & Urist, 1961) Under normal physiological conditions there exists a balance between resorption and replacement of the matrix If this view is accepted, it follows that the pathological resorption and replacement processes of otosclerosis might reflect a hormonal imbalance

Certain clinical observations of the pathogenesis and progress of otosclerosis are indicative of the involvement of hormones. The onset of otosclerotic deafness frequently coincides with puberty and the incidence of onset increases with age (Wullstein, 1960 Larsson, 1960) Since however the disease is histologically detectable long before it is clinically manifest (Larsson, 1960) the implication is that hormones may in some way enhance the progress of the disease This is supported by the observation that otosclerotic deafness seems more severe during pregnancy It is, of course, possible that this enhancement effect is only apparent since the patient normally has a heightened consciousness of body functions during this period.

The principal experimental approach toward ascertaining the significance of hormones in the pathogenesis of otosclerosis has been the measurement of levels of urinary steroids However studies of this type are few in number and results do not always agree. Herrmann & Maurer (1955) reported decreased levels of urinary androgens in otosclerotic patients, while Vyslonzil & Klein (1961) found these levels to be normal An increase in the level of urinary estrogens in otosclerotic patients, particularly in males aged 20 to 50 years, has been reported (Vyslonzil & Klein 1961 Vyslonzil 1963) More recently however DeJorge and co-workers (1965) found normal levels of estrogens in otosclerotics (both males and females) Changes" in the amounts of 17 ketosteroids

in which it is scientifically economical to proceed

All theories of the etiology of otosclerosis must ultimately center on the osteoid cell, in one or other of its forms, and on its deposition of intercellular material. Classically osteoblasts have been implicated in the initial deposition of bone; osteocytes, in its maintenance; osteoclasts, in its resorption. However the transformation of these three types of cells one into another and their ultimate common derivation from mesenchymal cells causes difficulties in determining the complement of activities which each performs and the division of labor between them, the latter possibly being less well-defined than originally supposed. Thus, any information that can be obtained about both the normal and abnormal physiology of these cells would be of immense value to research in otosclerosis. Tissue culture appears to be a logical and beneficial approach. Lawrence (1965) has been successful in isolating and growing osteoblasts from otosclerotic bone in tissue culture, but attempts at subculture have failed

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With respect to the second of these questions, the resorptive role has been variously attributed to the osteoclast and the osteocyte. As previously mentioned the latter has traditionally been assumed to participate in maintenance and turnover. But other evidence suggests that the osteocyte can resorb bone as well (Sognnaes, 1963). In electron micrographs of otosclerotic foci made by Chevance and co-workers (1969), lysis of collagen in the vicinity of osteocytes is invariably present, and, significantly, lysosomes occur within the osteocyte. Since the hydrolytic enzymes contained in lysosomes can dissociate protein, the simultaneous occurrence of these structures with pericellular lysis of collagen strongly implicates the osteocyte in the bone resorption which characterized the initial stage of otosclerosis. It is significant that large amounts of acid phosphatase (contained in lysosomes) have been detected histochemically in the matrix of otosclerotic foci (Albernaz & Covell, 1961). However the enzyme has also been found in large quantities in osteoclasts as well as in the bone matrix (Albernaz & Covell, 1961) and to this apparent contradiction we shall later return.

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	Level	Reference	Level	Reference	Level	Reference	Level	Reference
Calcium	Elevated	DeJorge	Lowered	Maurer	Normal	Soifer 1969 *b c*	Normal	Soifer
	Normal	Fowler			Lowered	Maurer		
	Lowered	Behrendt						
Phosphorus	Normal	Fowler Behrendt	Lowered	Maurer	Normal	Soifer	Normal	Soifer
	Lowered	DeJorge			Lowered	Maurer		
Iodine					Normal	Soifer	Normal	Soifer
Magnesium	Normal	Behrendt			Normal	Soifer	Normal	Soifer
	Lowered	DeJorge						
Copper	Normal	DeJorge			Normal	Soifer	Normal	Soifer
Chlorine	Normal	Behrendt DeJorge			Normal	Soifer	Normal	Soifer
Sodium	Normal	DeJorge			Normal	Soifer	Normal	Soifer
Potassium	Normal	Behrendt, DeJorge						
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Maurer's results indicating a lower than normal calcium and phosphorus content in endochondral bone (mallei incudes, semicircular canal promontory) from otosclerotics are in agreement with those of the above mentioned photon beam study They support the idea that alterations in elemental composition may be included among the "generalized" pathological ramifications of otosclerosis. Various ions in serum have been investigated with an eye to determining the extent of such generalized changes But as is evident from Table II conflicting results have but added additional pieces to the puzzle.

THE PRESENT STATE OF RESEARCH

The present state of research in otosclerosis appears to these authors to be one of productive confusion The varied approaches to the problem are building a foundation of data upon which a somewhat shaky superstructure of theory is precariously balanced It is advantageous for the solution of the problem that attacks are being made on so many fronts It has, however given rise to innumerable theories of the etiology of otosclerosis none of which attempts to integrate the findings of other approaches This state of affairs can be viewed in two lights. It is admirably scientific to be always aware of the limitations of one's discipline in order that foolish and misleading indiscretions of thought not be committed. But it is also both desirable and beneficial, if only for pinpointing inconsistencies, that some attention be devoted to consolidating, assessing, and placing in perspective the experimental data amassed from the various disciplines One would hope that a bit of reflection might suggest fruitful avenues for further experimentation as well as the general direction

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of embryonic cells, lysosomes can be stimulated to swell and rupture, thus releasing their contents, by simply oxygenating the culture (Sledge, 1965) It would appear to be significant that hyperaemia is an invariable condition in active otosclerotic foci Thus the theory is presented by Chevance and co-workers (1969) that the primary factor in the development of the otosclerotic focus *is a basic alteration in the osteocyte* resulting in the swelling and rupture of its lysosomes The latter by virtue of release of proteolytic enzymes, causes dissolution of the osteocyte and of the surrounding collagen fib-r ls

Since the osteoclast traditionally has been implicated in physiological resorption of bone and because of the presence of numerous osteoclasts in areas of otosclerotic resorption the hypothesis logically developed that the osteoclast was responsible for the resorptive processes *in the initial stage of the disease* No weak support was lent to this idea by the above mentioned discovery of intraosteoclastic acid phosphatase However Chevance and co-workers (1969) were unable to find evidence of activity (intracellular lysosomes and pericellular lysis of collagen) in any osteoclast observed under the electron microscope The role of the osteoclast may merely be phagocytic, a suggestion often forwarded but still lacking complete experimental substantiation During physiological resorption, osteoclasts exhibit intense succinate dehydrogenase and cytochrome oxidase activity while osteoblasts show only mild activity if any (Burstone, 1960 *a* *b*) An identical situation is found in otosclerotic resorption Albernaz & Covell (1961) find the activities of these enzymes to be intense in osteoclasts but mild or non-existent in osteocytes This high level of oxidative activity would be expected were the cell engaged in active phagocytosis And given the amount of acid phosphatase released into the matrix of the bone being resorbed, it would not be unusual to detect the enzyme within the osteoclasts as the latter engulfed remnants of the disintegrating matrix Finally because osteoclasts in otosclerotic foci exhibit no morphological or histochemical abnormalities, i e their appearance and activities are identical to those in physiological resorptive centers, it would seem unlikely that they are primary in pathogenesis of the disease.

The evidence which has accumulated for the primary role of the osteocyte in resorption at least hypothetically answers the second of our *two questions. The first* namely how are osteocytes stimulated to initiate resorption and subsequently to lay down fibrous bone is a considerably greater puzzle Regarding the initiation of resorption, a consideration which merits further attention is the above mentioned hyperaemia which is invariably present in active foci The fact that osteocytes are clustered around blood vessels in the focus (Alberti & Tarkannen 1963) may be significant

The deposition of fibrous bone following resorption however appears to result from an *alteration in enzyme activity in the osteocyte.* The enzymes which have been detected histochemically and/or biochemically in the focus are normally present in bone but the activities of certain of these, i e. lactate dehydrogenase and alkaline phosphatase are unlike those in uninvolved bone The decreased activity of lactate dehydrogenase in involved stapedes (Soifer et al 1969 *a*) may be linked with the increased quantity of free sulfhydryl groups found in the otosclerotic lesion (Chevance, 1965) Perhaps the enzyme is in some way depolymerized to yield subunits which are inactive. Alternatively the hyperaemia characteristic of active foci may be indicative of a hyperactive respiratory cycle. The latter could cause the observed decrease in lactate dehydrogenase activity via feedback inhibition

The role of alkaline phosphatase in otosclerosis would appear to be particularly significant for two reasons First, the experimental data show that it is present in large amounts in active foci (*Arslan & Ricci 1963* Chevance, 1965 Soifer et al., 1969 *a*) Second it is generally accepted that alkaline phosphatase functions in the formation of the normal bone matrix. The enzyme is implicated in the pro-

duction of collagen fibrils. Neuman (1956) proposed that phosphate esters, synthesized inside the cell, may be secreted at the cell surface where they are dephosphorylated by extracellular alkaline phosphatase and combine to form fibrils. This would explain the presence of the enzymes in the newly-formed matrix immediately prior to the deposition of bone salts as well as at fibrogenic sites. Alternatively or additionally alkaline phosphatase may function in the synthesis of the mucopolysaccharides of the ground substance. Kroon (1952) suggested that the enzyme may provide the units necessary for mucopolysaccharide synthesis by liberating the former from the hexose phosphate esters produced during glycolytic breakdown. A full and precise characterization of the role assumed by alkaline phosphatase in the pathogenesis of otosclerosis must await clarification of the physiological role of the enzyme as well as detailed definition of the changes in the matrix caused by the disease process.

FUTURE RESEARCH

Similarly the nature of the relationship between decreased lactate dehydrogenase activity and increased alkaline phosphatase activity has yet to be determined. Glycolytic substrates such as glucose-6-phosphate and D-glucosamine-6-phosphate are rapidly hydrolysed by non-specific alkaline phosphatase. The use of substrates labelled with ^{14}C and/or ^{32}P and the simultaneous determination of the activities of lactate dehydrogenase and alkaline phosphatase would seem a useful approach toward investigation of the functional relationship of the two enzymes.

Since evidence indicates that the content of collagen in otosclerotic bone is normal, turnover should be studied. The amount of bone present at any time is a result of two separate processes, resorption and accretion. Since otosclerosis results in an increase in the amount of bone (in stapes fixation) which appears to have a normal chemical matrix and inorganic composition, the equilibrium between the two processes must be altered in favor of accretion. Therefore, an investigation of this equilibrium by determination of absorption and accretion of the collagen matrix would provide relevant information.

Further there is positive evidence (the previously mentioned alternations in mallel, incudes, cortical bone, and vein see page 14) that otosclerosis may be a localized manifestation of a more generalized condition. Biochemical investigations in search of other aberrations in tissues, even those remotely located (for example, long bones) could conceivably be the approach most likely to be the key to the problem of otosclerosis.

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SUPPLEMENT 268

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BY

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ACTA OTO-LARYNGOLOGICA

SUPPLEMENT 268

The Face and Jaws after Surgical Experimentation with the Septovomeral Region in Growing and Adult Rabbits

BY

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CONTENTS

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I Introduction and Purpose

Normal development of body form is dependent upon the synchronous coordination of the activities of the growth sites of the skeleton and related structures (1) Any interference which alters the orderly progression of development results in faulty growth The subsequent deformity may vary and depends not only upon the type, intensity extent, and chronology of the noxious agent, but also upon the susceptibility and growth activity of the particular site. Trauma to endochondral growth centers can result in marked bony deformities This is in contrast to the effects of trauma to regions of sutural or appositional (periosteal, endosteal) growth of bones (2)

The septovomeral region is considered an important growth center (3 4) The relationship of trauma to this region to nasal and facial development is of clinical interest. A group of experiments was designed to test the effects upon growth of the face of varying degrees of surgical resection and trauma to different parts of the septovomeral region in both the growing and adult rabbit (5–11) The information obtained is reviewed and summarized in this report in relation both to basic concepts of growth of bones and to possible clinical significance.

II Review of the Literature

Hilton (3) in 1845 described the role of the vomer in the downward and forward growth of the maxillae and the deepening of the nasal fossae. Fick (12) in 1858 removed a portion of the cartilaginous nasal septum through a trephine opening of the nasal bones in growing dogs, cats, pigs, and goats. At autopsy the hard palate was greatly shortened anteroposteriorly and he stated that growth of the hard palate was dependent upon the growth of the nasal septum. Landsberger (13) in 1929 resected in part the anterior portion of the septum in dogs 2 weeks of age, killed them 6 months later and found that the anterior part of the floor of the nasal cavity was *higher* than normal. He concluded that the growing septum was *an important* factor in pushing the floor of the nasal cavity downward. Selman & Sarnat *reported that although the frontonasal suture* was a sit. of rapid growth (14), its extirpation in the rabbit failed to produce a growth arrest of the snout (15)

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The rabbit face is comprised, in part, of the mandibular premaxillary maxillary and nasal bones (Fig. 1)

The nasal cavity communicates posteriorly with the ventral surface of the skull by the choanae which, in the rabbit, are incompletely

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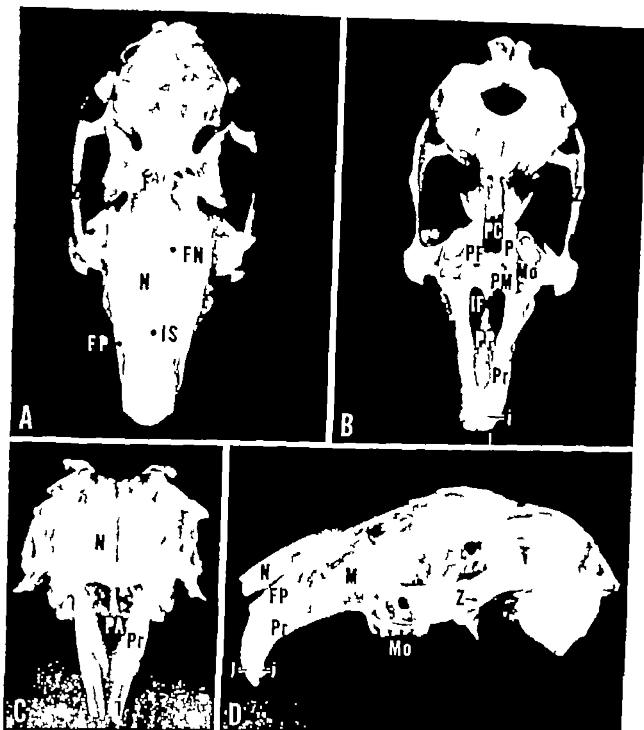
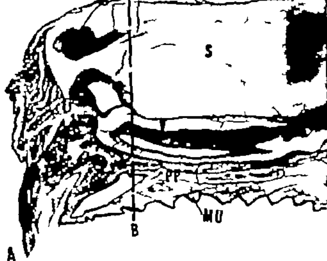


Fig 1 Photographs of normal adult rabbit cranium. *A* dorsal *B* ventral *C* frontal, *D* lateral views. *F* frontal bone *FN* frontonasal suture *FP* frontal process of premaxilla, *I* labial incisor *i* lingual incisor *IF* incisive foramen *IS* internasal suture *M* maxilla, *Mo* premolars and molars *N* nasal bone *P* palatine bone *PA* piriform aperture *PC* posterior choana *PF* palatine foramen *PM* palatine process of maxilla *PP* palatine process of premaxilla *Pr* premaxilla, *Z* zygomatic arch

divided (16) Anteriorly it opens to the outside by the piriform aperture

Bilateral division is effected chiefly through a median vertical cartilaginous plate the nasal septum (Fig. 2) This is continuous posterosuperiorly as a synchondrosis with a small crescentic vertical plate of bone the perpendicular plate of the ethmoid bone and posteroinferiorly with the presphenoid Both are sites of endochondral bone formation Inferopos



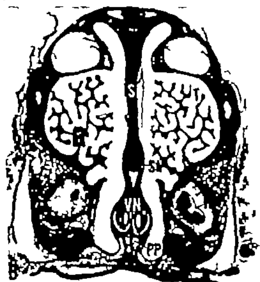


Fig 2 Photomicrographs of (*A*) sagittal, and (*B*) transverse (taken at approximately line *BB*) sections of snouts of 28-day-old unoperated rabbits. *I* labial incisor *i*, lingual incisor *IB* basal end of incisor *MU* palatal mucosa, *PP* palatine process of premaxilla, *S* septum, *SV* septovomeral joint, *T* maxilloturbinate *V* vomer *VN* vomeronasal organ (original 6). (From Wexler M. R., and Sarnat, B. G., Arch. Otolaryng., *74* 305–313 1961.)

teriorly the ventral portion of the cartilaginous nasal septum is supported by and rests in a dorsal groove of a vertical bony plate, the vomer This forms the septovomeral joint. The vomer a median, somewhat sickle-shaped vertical plate of bone separates the ventral portions of the nasal fossae. Anteriorly the nasal septum bears on its ventral margin, the paired enclosures of the vomeronasal organ. The septal cartilage extends anteriorly to the piriform aperture and terminates above the basal portion of the incisors (Figs. 2 *A* and 13). Information is meager on postnatal growth of the cartilaginous nasal septum (17 18) Normal levels of proliferative cellular activity in the young rabbit cartilaginous nasal septum were determined by autoradiographic studies with tritiated thymidine (18 *A*) Cellular activity was most pronounced in the anteroinferior and posterior zones (Fig. 3) The cartilaginous nasal septum exhibited an independent growth potential in organ culture (18 *B*)

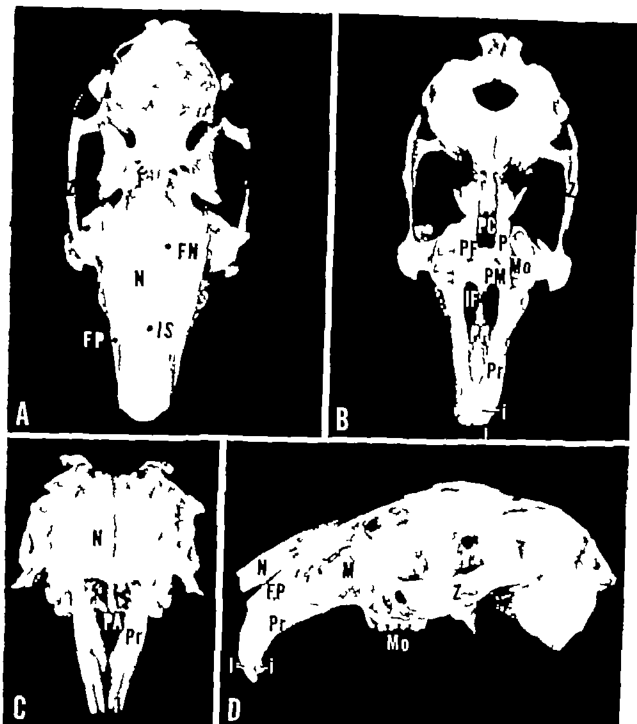


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foramen on the medial surface immediately behind the last molar

The body of the mandible bears on its dorsal margin the alveoli of an incisor anteriorly and of the premolars and molars posteriorly (Figs. 10 *E* and 16 *A*) The alveolar process of each premaxilla contains a larger labial and a smaller lingual incisor (Figs. 1 and 10 *E*) The alveolar process of each maxilla contains the premolars and molars. The double set of upper incisors and three upper premolars distinguish the rabbit as a lagomorph from the rodent. The upper incisor occludes labial to the lower one and represents a larger segment of a smaller spiral (Fig. 10 *E*) The lower incisor although larger than the upper one, represents a smaller segment of a larger spiral. While the incisors in the rabbit are continuously growing and erupting, they are worn at the edges and thereby maintain occlusion. Because of the thicker layer of enamel on the labial surface and the thinner layer of enamel and softer dentin on the lingual surface there is a differential in wear thus producing a sharp bevel. Whereas the basal end of the lower incisor extends to the premolar the basal end of the upper incisor is considerably anterior to the premolar (Fig. 10 *E*)

IV Materials and Methods

A Animals

Different experiments were designed to determine the effects of varying amounts of surgical resection and trauma to the septovomeral region in five groups of growing and one group of adult New Zealand albino rabbits (Table I) Additional rabbits served as operated and unoperated controls. The rabbit was selected because of the rapid increase in length of the snout.

B Anesthesia

A solution of 1 per cent procaine hydrochloride (0.5 to 2 cc) was injected submucosally in the sulcus between the upper incisors and lip The adult rabbits first were injected intramuscularly with pentobarbital sodium (30 mg/kg) and propiopromazine hydrochloride (Tranvet) (7.5 mg/kg)

C. Surgical Procedure

The animals were secured on an operating board in the supine position. The face and snout were cleansed with an antiseptic solution. An approximately 1.5 cm transverse incision was made through the mucosa between the upper incisors and the lip The tissues were elevated from the premaxilla, entrance was gained into the nasal cavity and the septum and septovomeral joint were exposed. This was the extent of the surgical procedure for the animals which served as operated on controls

In one experimental group of growing animals the inferior border of the cartilaginous nasal septum was mobilized, by lifting it out of the vomerine groove, and completely dislocated laterally (6) No tissue was resected. In a second group of growing rabbits central septal cartilage and mucous membrane sections ranging from 3 to 6 mm in width and 9 to 15 mm in length were resected with preservation of the surrounding borders (8) In a third group of growing animals maximum amounts of the anterior portion and body of the cartilaginous nasal septum including mucoperichondrium were resected (7) The vomer was left intact. A similar procedure was followed in a group of adult rabbits (9). In a final group of growing rabbits, cartilaginous nasal septum, vomer and premaxilla were removed (5). The mucosal wound margins were approximated and sutured with no 4-0 black silk. These animals, except for the one experiment with adult rabbits, were operated on at 2 to 7 weeks

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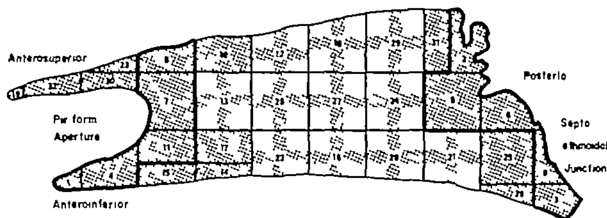


Fig 3 Diagrammatic representation of a longitudinal section of the cartilaginous nasal septum of a 3 week-old Dutch rabbit after intraperitoneal injection of tritiated thymidine The various zones are numbered according to their relative activity (labeling index, zone 1 3.36 zone 32, 0.35*). Anteroinferior and posterior areas (heavily outlined) were the most active Cell counts were made of the stippled areas. (From Long, R., Greulich, R., and Sarnat, B. G J Dent Res., *47* 505 1968)

The thin and elongated nasal bone forms the roof of the nasal fossa, and in conjunction with its fellow of the opposite side, the dorsal boundary of the piriform aperture (Fig. 1 *A*) The posterior border of the nasal bone articulates with the anterior border of the frontal bone forming the frontonasal suture, a secondary site of active growth in the young rabbit (14)

The maxillae form the main portion of the upper jaw Each maxilla consists of a central portion the body and of five processes—alveolar palatine orbital zygomatic, and sphenoorbital (Fig 1) The ventral portion of *the maxilla with the palatine bone forms the* hard palate (Fig 1 *B*) This structure is represented chiefly by a bony palatine bridge connecting the two sides of the skull between the premolars and molars It forms the roof of the oral cavity and a portion of the floor of the nasal cavity *Immediately in front of* it the palatine surface is perforated by a pair of large incisive foramina, which are broadly open to the nasal fossae (Fig 1 *B*) Laterally where the palatine bones articulate with the palatine processes of the maxillae are the palatine foramina.

The premaxilla forms the anterior part of the upper jaw It comprises a central portion, the body including the alveolar frontal and palatine processes (Fig. 1) The body forms a portion of the palatal surface of the skull and of the lateral boundaries of the incisive foramen The frontal process of the premaxilla a somewhat prominent narrow ridge extends posteriorly along the lateral surface of the nasal bone and articulates with the premaxillary process of the frontal bone (Fig. 1 *D*)

The mandible the largest element of the facial region, is composed of two portions united anteriorly by the symphysis (Fig. 5) Each half comprises a horizontal portion the body of the mandible, and a posterior *vertical portion the ramus.* The latter serves for the insertion of the muscles of mastication and for articulation with the skull The mandibular ramus forms a broad plate the lateral surface of which is occupied by the masseter muscle, while the medial surface *serves as an area of insertion for the pterygoid* muscles The surface of the ramus is greatly increased in its posteroventral portion through the expansion of the bone to form the angle The elongated articular surface is at the end of the condyloid process. Just inferior to this *on the anterior border* of the ramus is the coronoid process. The sigmoid notch is between these two processes. The nerve and vessels of the mandible enter at the mandibular

V Results

A Growing Rabbits

1 Resected septovomeral region and/or cartilaginous nasal septum (large amounts)

(a) Ante-mortem observations

As early as 4 days after resection of cartilaginous nasal septum there was a reversal of the incisal relationship, with the upper ones being lingual to the lowers. Subsequently the sharp incisal edge on the labial surface was not maintained. Marked overeruption and fractures of the incisors were frequent in the experimental animals with a longer postoperative survival. At times food would become lodged between the spread incisors. These factors sometimes made ingestion difficult. In a few of the experimental animals the weight was less and the fur was not as smooth when compared with the controls.

The face of the experimental rabbit was in marked contrast to the long, smoothly curved, tapered face seen in the operated and unoperated control animals (Fig. 4) The snout became progressively stubby along with the appearance of a pronounced indentation above the tip of the nose. This was suggestive of the face of a bull dog and was prominent less than 3 weeks postoperatively

(b) Post-mortem observations

Changes noted in the dissected skulls of the experimental animals were limited to the snout in the region anterior to the orbits, zygomas and molars. Although the findings were not always consistent, generally the degree of change varied directly with the amount of septum resected and the postoperative survival period.

The following description is characteristic of the most severe deformities seen in animals with the longest postoperative survival. The snout, when seen from the side, was tapered and shorter than that of the unoperated control. Whereas the snout in the control animal was the prominent part of the anterior face, this was reversed in the experimental rabbit. There was a marked deflection of the snout in a forward direction beginning anterior to the frontonasal suture This was in contrast to the smoothly curved dorsum of the control animals (Fig. 5) From below the palate and the incisive foramen were shorter (Fig. 6) From in front, the nasal aperture was smaller The snout when viewed from above was considerably shorter than that of the litter-mate control animal (Fig. 7)

The nasal bones were markedly shorter and narrower than those of the control animals and converged toward the premaxilla with nasal height and volume markedly reduced. The premaxilla and its frontal process were also shorter The end of the snout was tapered in the dorsoventral direction.

Examination of the parasagittally sectioned crania revealed in the experimental animals the extent of the septal defect in relation to the remaining septum and deformity of the snout and in the control animals the relation of the extent of the nasal septum to the snout. The site of the beginning of the downward deflection of the nasal bones was correlated with the posterior border of the septal defect which was anterior to the frontonasal suture (Fig. 8 *E*) Whereas in the control animal the nasal bones and hard palate were approximately parallel, in the experimental animal anterior projections of lines from the surfaces of these bones would soon intersect (Figs 8 *F F*) The post mortem gross findings of the facial skeleton at 18 35 55 91 and 131 days of age are summarized in Table II (Fig. 8)

The left (experimental, No. 14) and right (control, No 13) sides of the parasagittally sectioned skulls of litter-mate animals with the same survival period were approximated along the posterosuperior and occipital borders

Table 1 *Summary of various surgical experiments on the septovomeral region in growing and adult rabbits*

Surgical procedure	Number of animals: Control (operated and un-operated)	Number of animals: Experimental	Approx age at surgery (weeks)	Approx. post operative survival (weeks)	Type of study	Findings
Growing rabbits						
Resection of septo-vomeral region	6	18	4–7	17	Cross-sectional	Severe deformity of snout and incisors
Resection of large amount of cartilaginous nasal septum	10	15	3	15–21	Cross-sectional	Severe deformity of snout and incisors
Resection of large amount of cartilaginous nasal septum	7	26	2 and 3	1–21	Longitudinal	Gradual development of severe deformity of snout and incisors
Resection of linear horizontal segment of cartilaginous nasal septum	1	6	3	16	Cross-sectional	Moderate deformity of snout and incisors
Dislocation of cartilaginous nasal septum from vomerine groove	7	10	5–7	16	Cross-sectional	No deformity of snout and incisors. Deformity of septovomeral region
Adult rabbits						
Resection of large amount of cartilaginous nasal septum	8	9	Adult	16	Cross-sectional	No gross deformity of snout or incisors. Local defect of septum

of age weaned at 6 to 7 weeks of age, killed 16 to 20 weeks later and studied In addition, in another experiment, where large amounts of cartilaginous nasal septum were resected, th animals were studied at death from 4 to 145 days (11)

In most instances the animals were killed by injecting pentobarbital sodium into the heart Immediately after death the heads were severed from the body and a portion of the soft tissues was resected The heads were then fixed in either 70 per cent ethyl alcohol or 10 per cent formalin Subsequently further dissection was done and the heads were sectioned just to the left of the midline in the parasagittal plane with a small hack saw The skulls were never boiled since this would de stroy the remaining cartilaginous nasal septum

D Photographs and Roentgenographs

Ante-mortem and post mortem photographs were taken of the heads in the dorsal lateral frontal and parasagittal views Although every effort was made to obtain comparable photographs, this was not always possible.

Lateral roentgenographs were taken of the sectioned skulls with a standard roentgen apparatus at a target film distance of 100 cm operated at 50 and 100 mA, 58–68 kV and an exposure time of $^1/_2$ to $^3/_4$ of a second. Previous to this in some instances a barium sulfate paste thick enough to adhere to the margin of the surgical defect in the septum, was applied to outline the septal defect Tracings were made of selected roentgenographs.

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A. Growing Rabbits

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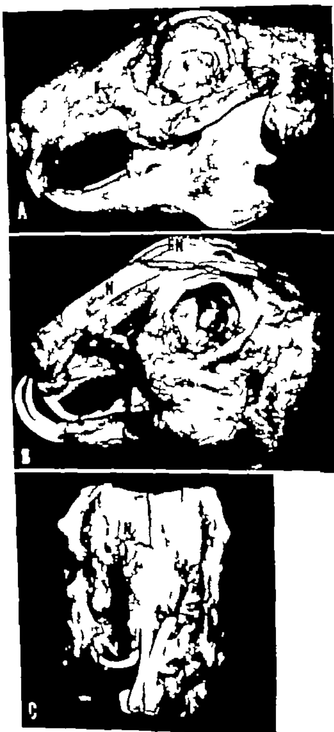


Fig 5 Post-mortem photographs of lateral view (*A*) of unoperated control rabbit No. 23 and lateral (*B*) and frontal views (*C*) of operated litter-mate rabbit No. 21 A portion of the septum and vomer were removed at 28 days of age. Postoperative survival was 118 days. Both animals were killed at 146 days of age. In (*B*) note the shorter snout, upper jaw and face, acute angulation, and peaking at the region of the fronto-nasal suture, *FN* and sharp downward direction of nasal bones, *N* Contrast this with the longer snout and smoothly curved dorsum of unoperated rabbit in (*A*). Also note malalignment and over growth of all incisors in (*B*) and (*C*). (From Wexler M. R., and Sarnat, B. G Arch. Otolaryng 305–313 1961)









(Fig. 9) Thus demonstrated the extreme differences in the size of the snouts

The upper incisors were usually in lingual occlusion with the lower incisors, the reverse of the normal. The upper and lower incisors were overerupted in marked malposition, fractured and deviated. The sharp labial bevel was frequently absent or reversed The post mortem gross dental findings at 18, 35 55 91 and 131 days of age are summarized in Table III (Fig. 8)

(c) *Roentgenographic observations*

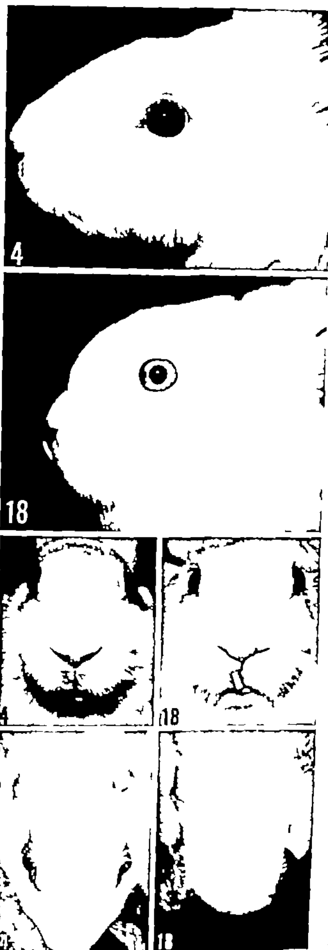
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In the experimental animals the anterior dorsum of the skull was flat in the younger animals With increase in postoperative survival this region was relatively shorter more posterior and closer dorsoventrally to the upper incisors than in the control rabbits (Fig. 11) Other findings in the experimental animals were larger pulpal cavities in the incisors, an increase in the proportion and amount of

Fig 4 Ante-mortem lateral, frontal and dorsal (retouched) view photographs of rabbit No. 4 in which a minor amount of the nasal septum was removed and of rabbit No. 18 in which a major amount of the nasal septum was removed at 1 days of age Note the marked contrast in facial appearance Animal No. 4 has a relatively normal, long, tapered face whereas animal No 18 has a short, stubby rounded face with an indentation above the nostrils (lateral view) and an overerupted lower incisor (From Sarnat, B. G and Wexler M R., Am. J Anat., *118* 755 767 1966)



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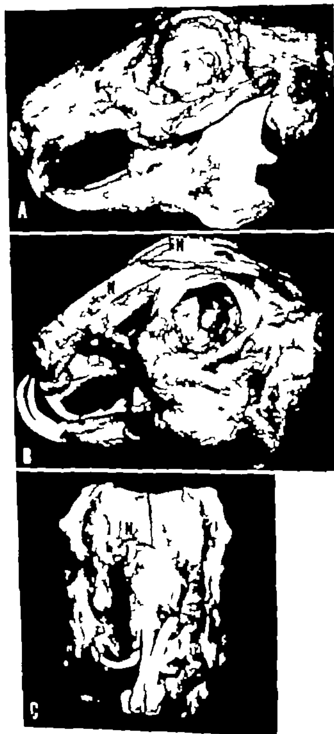


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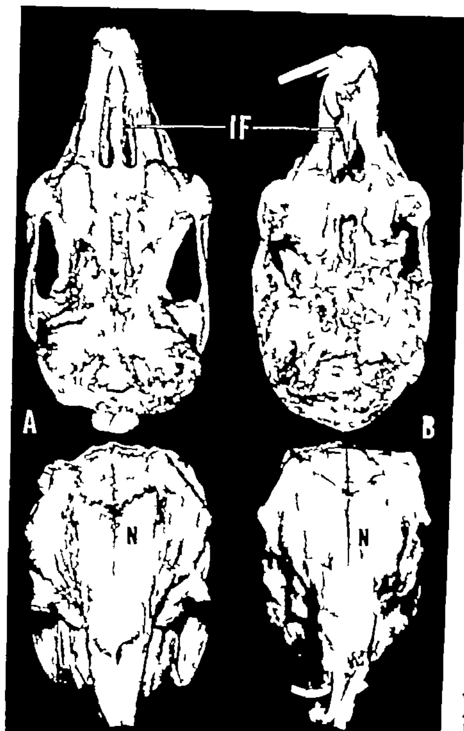


Fig 6 Post-mortem photographs of ventral (*upper*) and frontodorsal (*lower*) views of (*A*) unoperated control rabbit No. 3 and (*B*) operated on litter-mate No 1 In (*B*), note that the snout is shorter and broader *IF* incisive foramen is shorter in (*B*) N nasal bone Note again malalignment and overgrowth of incisors. (From Wexler M R., and Sarnat, B. G Arch. Otolaryng. 305–313 1961)

erupted to unerupted incisor and lesser amounts of alveolar bone supporting the incisors (Figs 10 and 11)

Tracings of the roentgenographs and superpositioning of these tracings further illustrated the differences (Fig. 12) The barium sulfate outlined surgical defect in the septum showed the relation to the surrounding area (Fig. 13) In the parasagittal view the basal end of the upper incisor was in close proximity to where a portion of the septum was resected

2. Resected linear segments of cartilaginous nasal septum

Ante-mortem a lack of forward growth of the upper face, sometimes associated with over eruption and malocclusion of the incisors, was

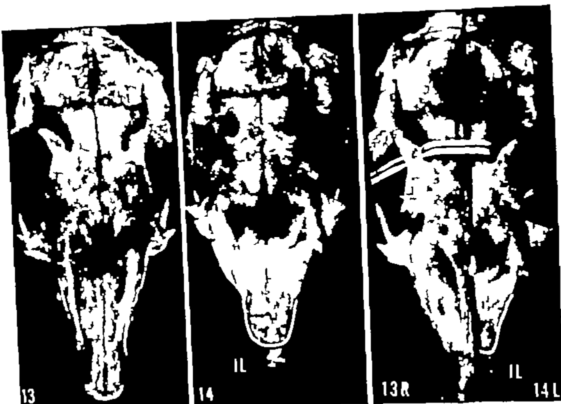


Fig. 7. Post-mortem dorsal view photographs of skulls of litter-mate rabbits No. 13 (operated control) and No. 14 (resected nasal septum) with postoperative survival of 110 days. In No. 14 note the marked lack of development of the snout. In the right-hand photograph, the right side of the skull of control rabbit No. 13 and the left side of the skull of experimental rabbit No. 14 were approximated along the postero-dorsal and occipital borders. Note that the differences are limited essentially to the snout area (see Figs. 9 and 12). *IL*, lower incisor. White outlines anterior part of snout. (From Sarnat, B. G. and Wexler M. R., Am. J. Anat., *118*, 755–767, 1966.)

noted within 6 weeks in some of the experimental animals. In one of the operated on control animals there was overeruption and malocclusion of the incisors but growth of the snout grossly did not appear to be affected. The findings in this group of experimental animals, although less extreme, were related to the findings in the animals with more extensive resection of cartilaginous nasal septum.

Post-mortem, in some animals, no or little septal defect was noted on cursory examination. Upon further study however and after the overlapping margins of the septum were retracted, the true extent of the septal defect could be evaluated (Fig. 14). The segment of cartilage resected was approximately 5×9 mm. At the time of death the size of the defect was approximately 3×16 mm. Note the relationship of the direction of the defect to the nasal bone and hard palate (Fig. 14 C).

3. Dislocated cartilaginous nasal septum

External gross examination of the snout, upper and lower jaws, and teeth disclosed no significant gross differences between the operated and unoperated animals. Examination of the transversely sectioned snouts revealed that the dislocated septal cartilage returned to its normal position or close to it so that continuity from the floor of the snout to the dorsum was re-established (Fig. 15). Lateral deviation and deformity of the septum and vomer were noted.

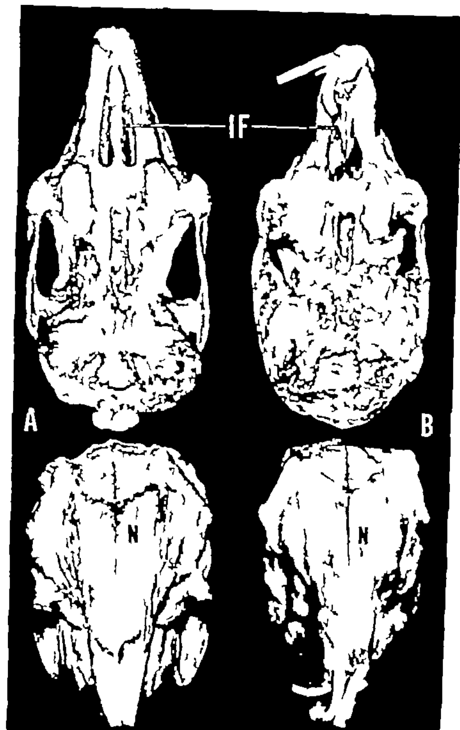


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	Age in days		
No	At oper	Postop surv	At death
8–14	14	4	18
8–22	21	14	35
8–25	21	34	55
8–20	21	70	91
3–14	21	101	131
3–13	—	—	131

Table 2. *Post-mortem gross and roentgenographic findings of the face in selected rabbits 18 to 131 days of age after resection of cartilaginous nasal septum (see Figs 8 10 and 11)*

Number	Age at death (days)	Postop. surviv (days)	Antero-posterior curvature dorsal surface of snout	Size of nasal aperture	Relation of anterior border of nasal bone to upper incisor		Palatal length (from medial surface of upper first premolar to lingual incisal alveolar crest)	Relation of upper face to mand ble
					anteriorly	superiorly		
8–14	18	4	Within normal range	Within normal range	Within normal range	Within normal range	Within normal range	Within normal range
8–22	35	14	Slight flattening	Within normal range	May be somewhat less than normal	Within normal range	May be somewhat less than normal	Upper face somewhat less prominent
8–25	55	34	Loss of anterior curvature	Less than normal, soft tissue depression above upper incisal area	Less than normal	Decrease	Decrease	Upper face somewhat less prominent
8–20	91	70	Marked depression of anterior border	As above but more marked	Considerable decrease	Decrease	Decrease	Upper face markedly less prominent
3–14	131	110	Severe depression of anterior border	As above but more severe	Severe decrease	Severe decrease	Severe decrease	Upper face severely less prominent

From Sarnat, B. G and Wexler M R., Brit. J Plast. Surg 22 313-323, 1969

B Adult Rabbits

Resected cartilaginous nasal septum (large amounts)

Ante-mortem observations of the snout and incisors revealed no gross differences between the control and experimental rabbits. In a few of the latter group a clear nasal discharge was noted at times. Post mortem gross examination of the lateral and parasagittal views of the face jaws, and incisors likewise showed no gross differences between the control and experimen

Fig 8 Post-mortem photographs, arranged accord ng to postoperative survival, of parasagittally sectioned skulls of rabbits which had cartilaginous nasal septum resected at 14 or 21 days of age with a post operative survival of 4 to 110 days. Note the flatness of the anterior dorsum in (*A*), (*B*) and (*C*) with some deflection in (*D*) and more marked deflection in (*E*). Also note in (*A*) that the upper incisal edge is just lingual to the lower one. With the increase n postoperative survival (*B C D* and *E*) the discrepancy becomes greater as does the overeruption of the incisors. When the clinical crown of the incisor becomes quite long, it may fracture (*F*), operated control rabbit which had the preliminary surgical procedure but no cartilaginous nasal septum resected Note the length of the snout, the smoothly curved dorsum, the length and position of the nasal bone the extent of the intact cartilaginous nasal septum and the form, position and relationship of the incisors in contrast to experimented on litter-mate n (*E*) The nasal bones converge in an anterior direction toward the palate in the animals with severe deformity (*E*) whereas in the operated control animals the nasal bones tend to remain parallel (*I*) as indicated by the black dashes. *d* septal defect *FN* frontonasal suture *S* septum See Figs. 10 and 11 (From Sarnat, B G and Wexler M R Brit. J Plast. Surg 22 313 323 1969)

Table 3. Post-mortem gross and roentgenographic dental findings in selected rabbits 18 to 131 days of age after resection of cartilaginous nasal septum (see Figs 8, 10 and 11)[a]

Number	Age at death (days)	Postop. survival (days)	Relationship and occlusion of upper and lower incisors	State of incisal eruption	Fracture of incisors	Lateral deviation of incisors	Incisal bevel	Pulpal size	Alveolar bone supporting incisors
8-14	18	4	Relationship slightly reversed from normal upper incisors just lingual to lowers but in occlusion	Within normal range	0	0	Within normal range	Within normal range	Within normal range
8-22	35	14	Upper incisors definitely lingual to lower incisors and not in occlusion	Over eruption	0	0	Within normal range	Within normal range	Within normal range
8-25	55	34	Upper incisors markedly lingual to lower incisors and not in occlusion	Marked over eruption	Occasional		Some reversal from normal with lingual surface more prominent	Some increase over normal	Considerably less than normal
8-20	91	70	Upper incisors markedly lingual to lower incisors and not in occlusion	Marked over eruption	Not unusual	+ +	Increased reversal	Further increase	Considerably less than normal
9-14	131	110	Upper incisors markedly lingual to lower incisors and not in occlusion	Less apparent because of fractures	Frequent	+ + +	Frequent reversal or absent	Considerable increase	Considerably less than normal

[a] From Sarnat, B. G. and Wexler, M. R., Brit. J. Plast. Surg. 22, 313-323, 1969.

The response to resection of cartilaginous nasal septum varied with the age of the rabbit, the amount (and site) resected as well as the duration of the postoperative survival. Although an attempt was made to standardize the surgical procedure, the same amount of cartilaginous nasal septum was not resected from comparable sites in all animals. The degree of change varied from relatively little to marked, depending on these factors. Severe deformities involving many lateral facial structures were produced by removing portions of this midline structure, the cartilage of the nasal septum.

In a few animals which expired at the time of, or shortly after surgery, post-mortem examination revealed that approximately 60 to 75 per cent of the cartilaginous portion of the septum was removed. In animals with a 4 month postoperative survival, the surgical defect represented approximately only 30 to 40 per cent of the septum. The defect may have *remained nearly* the same in actual size but proportionately it became smaller with continued growth of the cartilaginous nasal septum. Histologic investigation of the septal border may provide information regarding the regenerative activity *at this site*.

Questions arose as to the role of the cartilaginous nasal septum and its sites of activity in relation to growth and form of the snout. *Is* the snout deformity a result of lack of growth of the cartilaginous nasal septum or lack of support? In one experiment, central horizontal *segments*, *3–6* mm wide and 9–15 mm long, of cartilaginous nasal septum



Fig 9 Post mortem lateral view photographs of left parasagittally sectioned skulls of litter mate rabbits No 13 (operated control) right side and No. 14 (resected nasal septum) left side approximated along the posterodorsal and occipital borders for contrast with a postoperative survival of 110 days (see Figs. 7 and 12) In rabbit No. 13 note the length of the snout and the smoothly curved dorsum. In rabbit No. 14 note the markedly underdeveloped snout, the downward angulation of the nasal bone in an anterior direction and the smaller nasal aperture. White line denotes anterior part of skull of experimental rabbit No 14 Note that in an anterior direction the nasal bone converges toward the palate See Fig. 12 (From Sarnat, B G and Wexler M R. Am. J Anat *118* 755 767 1966)

tal rabbits (Fig 16) Inspection of the right half of the left parasagittally sectioned skulls disclosed a large defect of the cartilaginous nasal septum in the experimental animals (fig. 16 *B*) *No unusual deflection of the nasal* bones was noted.

VI Discussion

A The Face and Jaws after Surgical Experimentation with the Septovomeral Region

Young rabbits were used to impose injury during a period of rapid growth It was demonstrated that resection of the septovomeral region in growing rabbits *elicited a prompt and early response manifested by a deceleration of* growth of adjacent bones A similar response was obtained, moreover when large amounts of only cartilaginous nasal septum were resected with particular care taken not to injure the septovomeral joint The severity of the growth arrest became strikingly apparent with a longer postoperative survival

Ante mortem the snout of the unaffected animal was long and tapered with a smoothly curved dorsum (Fig. 4 No 4) This was in contrast to th snout of the affected animal which was short, stubby rounded with a sharp *deflection of the dorsum in an anterior direction and an indentation above the nostrils* (Fig 4 No 18) Post-mortem the dissected skull of the control animal had an appearance comparable with ante mortem *This was not as true* with the experimental animal because the soft tissue masked *the findings*

No.	Age in days At opar	Age in days Postop. surv	Age in days At death
8–14	14	4	18
8–22	21	14	35
8–25	21	34	55
8–20	21	70	91
3–14	21	110	131

F g 11 Reproduction of lateral roentgenographs, arranged according to postoperative survival, of parasagittally sectioned skulls of rabbits which had cartilaginous nasal septum resected at 14 or 21 days of age with postoperative survival of 4 to 110 days. Note the flat anterior dorsum with increasing downward deflection in an anterior direction with increasing postoperative survival. The deflection begins at the posterior site of resection. Contrast these with control animals in Fig. 10. Note the shorter snout, nasal bone and palate and the smaller piriform aperture. Also note in (*A*) that the upper incisal edge is just lingual to the lower one. This is more marked in the animals with longer postoperative survival. Also in contrast with Fig. 10 the incisors are markedly overerupted and longer and not in occlusion. *IL*, lower incisor *IU* upper incisor *Me* premolars and molars; *N* nasal bone *O* orbit; *P* palate; *PA* piriform aperture; *PU* pulpal cavity (From Sarnat, B. G., and Wexler M. R., Brit. J Plast. Surg., 22, 313–323 1969)

No.	Age in days at death
6–11	19
6–15	37
3–4	52
1–12	95
3–13	131

Fig 10 Reproduction of lateral roentgenographs, arranged according to ge from 19 to 131 days at death, of parasagittally sectioned skulls of rabbits with the cartilaginous nasal septum ntact. Note the downward smooth cu e of the terior dorsum the length and anterior extension of the nasal bone the size of the piriform aperture the length of the palate the form, position and relationship of the incisors, *IL* lower incisor *IU* upper labial and lingual incisors, *Mo* premolars and molars N nasal bone *O* orbit *P* palate *PA* piriform aperture *PU* pulpal ca ity Contrast these with experimental animal in Fig. 11 (From Sarnat, B. G and Wexler M R Brit. J Plast Surg., *22* 313 3-3 1969)

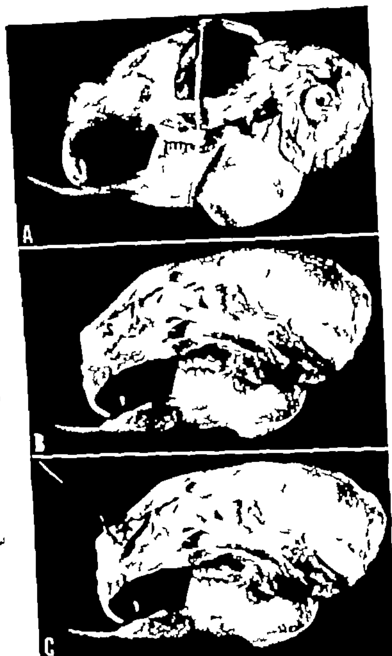


Fig 14 Post-mortem lateral (*A*) and parasagittal view (*B* *C*) photographs of skull f rabbit No. 2 which had an approximately 5 9 mm segment of septal cartilage resected at 21 days of age and was killed at 133 days of age. In (*A*), note the shorter nar rower snout and the declination of the dorsum in an anterior direction so that it converges toward the palate as compared with unoperated control animal in Fig. 5 *A* Also note the marked over growth and malocclusion of the incisors. In (*B*), no significant septal defect is noted, but in (C) the cartilaginous overlap, *X* is retracted and an oblique linear septal defect approximately 3 16 mm is obvious. *S* cartilaginous nasal septum. See Fig. 8 (From Sarnat, B. G and Wexler M. R., Acta Otolaryng., 63 467–478, 1967)

sociated trauma to the vomer and the septovomeral joint in growing rabbits failed to produce any significant gross changes in the external shape and size of the snout, jaws, or teeth The dislocated septal cartilage returned to its normal position, or close to it, re establishing the continuity from the floor of the snout to the dorsum. There were varying degrees of septal and septovomeral deformity (Fig. 15) The effects of permanent dislocation without vomeral contact were not determined

These experiments suggest that the deform-

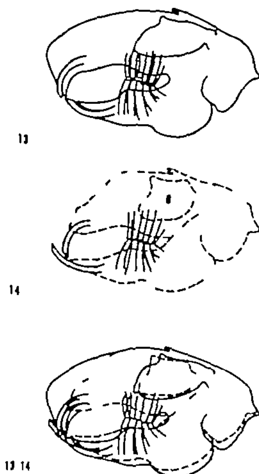


Fig 12 Approximate tracings (original by Dr Herbert Muehnle) of lateral roentgenographs of right side of parasagittally sectioned skulls of litter-mate rabbits killed at 131 days of age In control animal No. 13 note the general size shape, and regularity of the face, jaws and incisors. In experimental animal No. 14 the nasal cartilaginous septum was resected at 21 days of age Note the smaller size the different shape the irregularity of the upper face and *O* smaller orbit. In the lowermost illustration, the tracings were superposed along the posterodorsal and occipital borders to contrast the differences between the control and experimental animals. See Figs. 9 10 *E* and 11 *E* (From Sarnat, B G and Wexler M R., Am. J Anat., *118* 755 767 1966.)

were resected in growing rabbits (8) After a postoperative survival of 16 weeks a deformity of the snout was noted but it was less than in animals in which larger amounts of cartilaginous nasal septum were resected At post mortem, an overlap of septal borders was noted at the operative site (Fig 14 *C*) These findings were interpreted as a dissipation of the growth force of the cartilaginous nasal septum at the site of resection with a resulting lack of forward and dorsal growth of the snout.

In a different experiment large amounts of cartilaginous nasal septum were resected in adult rabbits (9) After a postoperative survival of 16 weeks, study of the dissected skulls showed a large septal defect but no deformity of the snout (Fig. 16 *B*)

Deliberate dislocation of the septum with as-



Fig 13 Roentgenograph of parasagittally sectioned cranium of operated on rabbit No 20. Note radiopaque outline of *d* septal defect the border of which was painted with barium sulfate paste *IU* upper incisor (From Wexler M R and Sarnat, B. G Arch. Otolaryng *74* 305 313 1961)

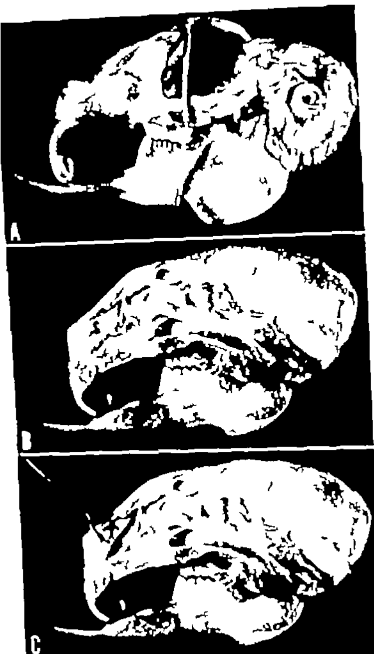
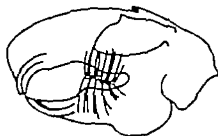


Fig 14 Post-mortem lateral (*A*) and parasagittal view (*B* *C*) photographs f skull of rabbit No. 2 which had an pproximately 5 9 mm segment of septal cartilage resected at 21 days of age and was killed at 133 days of age. In (*A*), note the shorter narrower snout and the declination of the dorsum in an anterior direction so that it converges toward the palate as compared with unoperated control animal in Fig. 5 *A* Also note the marked overgrowth and malocclusion f the incisors. In (*B*), no significant septal defect is noted, but in (*C*) the cartilaginous overlap, *X* is retracted and an oblique linear septal defect approximately 3 16 mm is obvious. *S*, cartilaginous nasal septum. See Fig. 8 (From Sarnat, B. G and Wexler M R., Acta Otolaryng., *63* 467–478, 1967)

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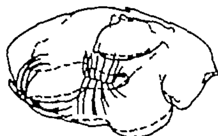
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13



14



13 14

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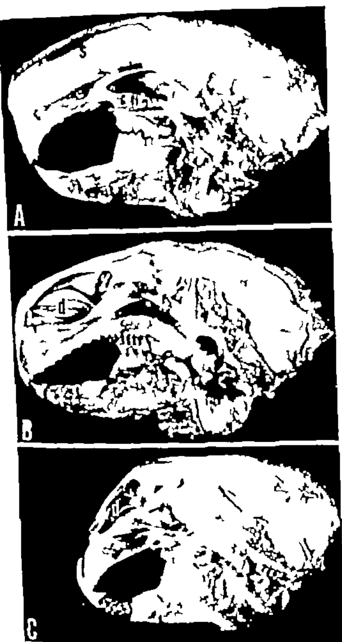


Fig 16 Post mortem photographs of right halves of left parasagittally sectioned rabbit skulls. (*A*), operated control animal No 13 No cartilaginous nasal septum was resected. (*B*) cartilaginous nasal septum was resected in this experimental animal N M—1 when it was an adult. Compare with (*A*) and note similarities of size, shape and regularity of incisors. Also note regularity of dorsal curvature uninfluenced by underlying septal defect, *d* (*C*) cartilaginous nasal septum was resected in this experimental animal No. 11 at 3 weeks of age and killed at approximately 4 months of age. Note growth arrest of snout and malocclusion of incisors. Also note deflection of snout in an anterior direction beginning in the region of septal defect, *d*. *S* septum. (From Sarnat, B. G and Wexler M R. Arch. Otolaryng., 86. 463–466, 1967.)

large amounts of cartilaginous nasal septum were resected (6, 9) Consequently it was concluded that the malocclusion was related to failure in anterior growth of the snout and not to trauma to the growing tooth at the time of the original surgery Malocclusion may occur on an inherited basis (19) Injury to growing rodent incisors may lead not only to overeruption but also disturbances in enamel formation (20) The latter was not found in this experiment.

Along with these face, jaw and dental abnormalities it is possible that there were other anatomic and physiologic alterations of the nose, temporomandibular joints and the rest of the masticatory and respiratory systems.

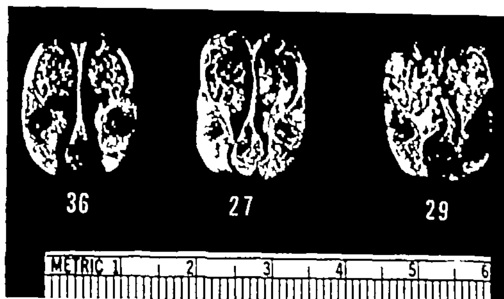


Fig 15 Post-mortem photographs of transverse sections of rabbit snouts at the level of the basal end of the incisors of rabbit No 36 an unoperated control and rabbits No 27 and No. 9 *in which the* septum was dislocated laterally Note the lateral deviation of the septum in No. 7 and the more marked deformity of the septum and vomer in No. 29 No external deformity of the snout was noted. (From Wexler M R., and Sarnat, B. G Arch. Otolaryng., *81* 68 71 1965)

lty of the snout after resection of cartilaginous nasal septum in growing rabbits is the result *of a lack of growth rather than a lack of sup*port of the cartilaginous nasal septum. Another possible cause of deformity is that of scar tissue resulting from the surgical procedure On the basis of the above evidence this is not considered to be a factor

Increase of the cartilaginous nasal septum in height, length and thickness is by both interstitial and perichondrial growth The relative contributions of each is not known A study of the proliferative activity of chondrocytes with tritiated thymidine indicated the highest activity to be in the anteroinferior and posterior parts of the cartilaginous nasal septum (18 *A*) *Although the central zone of the cartilaginous* nasal septum had a relatively low rate of proliferation, this rate would result in doubling of the cell population in about 4 weeks. Assuming that a significant increase in septal mass accompanies increased chondrocyte numbers then deformities of the snout might well be anticipated as a consequense of surgical ablation of the central zone early in life

B Dental Changes

Concomitant with lessened growth of the snout a relative mandibular prognathism resulted with lack of occlusion of the upper and lower incisors The incisors overerupted in bizarre forms as a result of continuous growth and eruption coupled with a decreased rate of attrition The relation of the upper incisors lingual to the lower ones and overeruption of the incisors proved to be early clinical signs of a developing deformity of the snout. This was noted as early as 4 days postoperatively In other experimental rabbits where snout length was not as severely affected, occlusion was relatively normal

Another possible cause for this deformity is that the basal ends of the incisors, adjacent but lateral to the septovomeral region were traumatized at the time *of surgery No dental* deformities were noted (i) in the operated control animals in which the surgical procedure was carried out up to removal of cartilaginous nasal septum (ii) in rabbits in which the cartilaginous nasal septum was dislocated but not resected (6) or (iii) in adult rabbits in which

movement of the face (1 2, 4 27–32) Although each of these regions exemplifies endochondral bone growth, the histologic arrangement of the adjacent tissues differs (31) These differences account for some of the variations in growth of different bones (33)

Surgical removal of the sphenooccipital synchondrous growth center in rats produced a shorter skull (34) The changes in form were limited mostly to the posterior half of the neurocranium, both base and vault. None was noted in the fac- jaws or teeth.

2. Secondary growth sites

Growth of bones is also active at secondary or accommodating growth sites (4 22, 35). Appositional growth, as well as modeling resorption occurs on the surfaces of bones (periosteal and endosteal) and contributes to growth and movement in all directions Sutural growth is found only in the skull. Growth of the cartilaginous nasal septum influences sutural growth and contributes to downward and forward growth of the face and palate (28). The contents of certain other cavities of the skull likewise influence the growth of a complex of adjoining bones and sutures Examples are the brain and the neurocranium, the orbital contents and orbit, the tongue and the oral cavity Muscle activity local and regional, also plays an important role

In growing rabbits, considerable growth of bones occurred at the frontonasal suture (14) The nasal side contributed approximately twice the amount that the frontal side contributed. Extirpation of this suture however did not affect grossly growth of the snout (15) Similarly in growing monkeys extirpation of the midpalatine and transpalatine sutures resulted in no gross alterations in either facial or jaw growth (36)

Subsequent to resection of the cartilaginous nasal septum, the nasal bones were found to be shorter than those of the control animals. With less impetus from growth of the cartilaginous nasal septum no doubt secondary activity at the frontonasal suture was reduced. This change in activity at the frontonasal suture could be studied by means of radiopaque implants and serial roentgenographs.

D Clinical Considerations

Findings in experimental animals may be of assistance in understanding normal and abnormal growth of bones in the human being. Deformities of the nasal septum and associated structures seen clinically in the adult have been considered manifestations of severe nasal injury incurred during an earlier period. Since the above experimental findings confirm this thesis, it would be advisable that young children, who have sustained injuries to the cartilagineous septum and nose, be treated and observed not only for the immediate but also for late deformities. In addition they should be followed for deformities of the teeth, jaws and face

In a child with a complete bilateral cleft palate, the upper face may be unable to obtain a full expression of downward and forward growth because of lack of contact of the palatal shelves with the ventral-free actively growing septovomeral region (Fig. 17) Furthermore, trauma to the septal region, during cleft palate or septal surgery might have an untoward effect upon growth of the nose and upper jaw and face. Injury to the midpalatine or transpalatine sutures which are secondary growth sites, is of less import (36).

In surgical procedures related to the nasal bones and septum in the actively growing child one would not anticipate a growth arrest in relation to trauma to the nasal bones. Some deficiency of growth might result, however if there were sufficient trauma to the cartilaginous nasal septum. This statement in regard to differential reaction is based upon the absence of gross deformity of the snout in rabbits after either extirpation of the frontonasal suture or temporary dislocation of the nasal septum but the presence of deformity of the snout after resection of cartilaginous nasal septum (37).

C Growth of Bones

The dynamics of the growth of bones are complicated (1) The basic pattern of a bone is inherent. The form and architecture may be modified however during prenatal and postnatal growth by local regional and systemic influences acting through the internal and external environments The end result, at any given time, is a record of the effects of all the vicissitudes

A great deal has been learned about the prenatal and postnatal etiology of facial and other abnormalities in the experimental animal The material of this report is only part of a series of experiments in which the relationship of injury to postnatal growth has been studied (1 2, 21 22) Throughout our lives we are constantly reacting to our environment. Variations in temperature light humidity atmospheric pressure terrestial and extraterrestial radiation and gravity affect us In addition the vast number of toxic agents, intentionally or unintentionally ingested in our food (or essential deficiencies) and water and inhaled in our air determine our destinies. Consider the effect of our environment upon the skeletal growth sites and the resulting changes in size and shape of the jaws face, and body

There are many mechanisms (nervous, hormonal metabolic, enzymatic) by which the environment directly induces adaptive changes (23) Environmental stresses can interact either directly such as variations in temperature and oxygen or indirectly with the genetically controlled enzyme forming system. There is no evidence that environmental stresses can induce genetic change Rather the stress permits such genetic changes as may occur in natural mutations to be realized and fixed

Young rats exposed to cold stress had a smaller skull a longer face in relation to the cranial vault a narrower nose a rounder neurocranium and a shorter femur (24) Natives living at high altitudes and exposed to the environmental stresses of hypoxia and cold have a slower postnatal growth and lesser adolescent growth spurt than other groups (25) On earth gravity is considered normal or 1 0 g. What skeletal and other changes will occur in environments of hypogravity (moon 0 18 g) or hypergravity (Jupiter 2 65 g)? These and other factors are of great interest to the new field of cosmic biology and should be of concern to us as surgeons

A basic physiologic concept is that throughout life bone is in a continuous state of apposition and resorption along periosteal and endosteal surfaces Consequently skeletal size and shape are always subject to change When the skeletal mass increases, as in children, apposition is more active than resorption Endochondral and sutural growth are active When the skelet mass is constant as in the adult, apposition and resorption although active are in equilibrium Endochondral and sutural growth have ceased. When the skeletal mass decreases, as in old age resorption is more active than apposition

Of the three modes of postnatal growth of bones, endochondral may be considered to be primary The other two, appositional (and resorptive) and sutural may be considered to be secondary The skull has proved to be a rich source of study since nowhere else in the body are representatives of all of these different sites found. As a result of the activities of these sites the facial skeleton increases in size in all three planes—height, width and length But it grows in these three dimensions differentially at different times and at different rates (14 26 27 28)

1 Primary growth centers

Primary endochondral centers of growth are epiphyses in the long or tubular bones, the costochondral junction of ribs and the clavicle Some of those in the skull are the sphenoethmoidal and sphenooccipital synchondroses, the septoethmoidal and septopresphenoid joints, and mandibular condyle These centers contribute to the downward and forward growth and

movement of the face (1 2, 4 27–32) Although each of these regions exemplifies endochondral bone growth, the histologic arrangement of the adjacent tissues differs (31) These differences account for some of the variations in growth of different bones (33)

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D Clinical Considerations

Findings in experimental animals may be of assistance in understanding normal and abnormal growth of bones in the human being. Deformities of the nasal septum and associated structures seen clinically in the adult have been considered manifestations of severe nasal injury incurred during an earlier period Since the above experimental findings confirm this thesis, it would be advisable that young children, who have sustained injuries to the cartilaginous septum and nose, be treated and observed not only for the immediate but also for late deformities. In addition they should be followed for deformities of the teeth, jaws and face.

In a child with a complete bilateral cleft palate, the upper face may be unable to obtain a full expression of downward and forward growth because of lack of contact of the palatal shelves with the ventral-free actively growing septovomeral region (Fig. 17) Furthermore, trauma to the septal region, during cleft palate or septal surgery might have an untoward effect upon growth of the nose and upper jaw and face Injury to the midpalatine or transpalatine sutures which are secondary growth sites, is of less import (36)

In surgical procedures related to the nasal bones and septum in the actively growing child one would not anticipate a growth arrest in relation to trauma to the nasal bones. Some deficiency of growth might result, however if there were sufficient trauma to the cartilaginous nasal septum. This statement in regard to differential reaction is based upon the absence of gross deformity of the snout in rabbits after either extirpation of the frontonasal suture or temporary dislocation of the nasal septum but the presence of deformity of the snout after resection of cartilaginous nasal septum (37)

C Growth of Bones

The dynamics of the growth of bones are com plicated (1) The basic pattern of a bone is inherent. The form and architecture may be modified however during prenatal and post natal growth by local, regional and systemic influences acting through the internal and ex ternal environments. The end result, at any given time is a record of the effects of all the vicissitudes

A great deal has been learned about the prenatal and postnatal etiology of facial and other abnormalities in the experimental animal. The material of this report is only part of a series of experiments in which the relationship of injury to postnatal growth has been studied (1 2 21 22) Throughout our lives we are constantly reacting to our environment Varia tions in temperature, light, humidity at mospheric pressure, terrestial and extrater restial radiation and gravity affect us In addition the vast number of toxic agents intentionally or unintentionally ingested in our food (or essential deficiencies) and water and inhaled in our air determine our destinies Consider the effect of our environment upon the skeletal growth sites and the resulting changes in size and shape of the jaws, face, and body

There are many mechanisms (nervous, hor monal metabolic, enzymatic) by which the en vironment directly induces adaptive changes (23) Environmental stresses can interact either directly such as variations in temperature and oxygen, or indirectly with the genetically con-trolled enzyme forming system There is no evidence that environmental stresses can in duce genetic change. Rather the stress permits such genetic changes as may occur in natural mutations to be realized and fixed.

Young rats exposed to cold stress had a smaller skull a longer face in relation to the cranial vault, a narrower nose, a rounder neurocranium and a shorter femur (24) Na tives living at high altitudes and exposed to the environmental stresses of hypoxia and cold have a slower postnatal growth and lesser adolescent growth spurt than other groups (25) On earth gravity is considered normal or 1 0 g. What skeletal and other changes will occur in environments of hypogravity (moon 0 18 g) or hypergravity (Jupiter 2 65 g)? These and other factors are of great interest to the new field of cosmic biology and should be of con cern to us as surgeons

A basic physiologic concept is that through out life bone is in a continuous state of ap-position and resorption along periosteal and endosteal surfaces Consequently skeletal size and shape are always subject to change When the skeletal mass increases, as in children, ap-position is more active than resorption. Endo-chondral and sutural growth are active When the skelet mass is constant as in the adult, apposition and resorption although active, are in equilibrium Endochondral and sutural growth have ceased. When the skeletal mass decreases, as in old age resorption is more active than apposition

Of the three modes of postnatal growth of bones, endochondral may be considered to be primary The other two appositional (and re sorptive) and sutural may be considered to be secondary The skull has proved to be a rich source of study since nowhere else in the body are representatives of all of these different sites found. As a result of the activities of these sites the facial skeleton increases in size in all three planes—height, width and length But it grows in these three dimensions differentially at different times and at different rates (14 26 27 28)

1 Primary growth centers

Primary endochondral centers of growth are epiphyses in the long or tubular bones, the costochondral junction of ribs and the clavicle Some of those in the skull are the sphenoeth-moidal and sphenooccipital synchondroses, the septoethmoidal and septopresphenoid joints, and mandibular condyle These centers contrib-ute to the downward and forward growth and

that of the orbital contents to the growth of the orbit and the brain to the growth of the neurocranium.

When lesser amounts of cartilaginous nasal septum were resected (linear horizontal segments), the snout and dental deformities were also less pronounced. After temporary lateral dislocation of the cartilaginous nasal septum neither snout nor dental abnormalities were noted. All of the above were done in young rabbits. When large amounts of cartilaginous nasal septum were resected in adult rabbits, neither snout nor dental changes were observed.

The cartilaginous nasal septum is important in the growth and development of the upper face of the rabbit. This information if applicable to human beings is of particular clinical significance in young patients with injuries to this area or with bilateral complete cleft palates.

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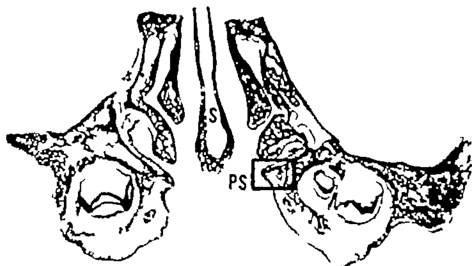


Fig 17 Frontal section through the upper jaw of a newborn human being with bilateral cleft palate *PS* palatine shelf *S* septum. See Fig. – (From Weinmann, J P Sarnat, B G and Sicher H Oral Surg., Oral Med and Oral Path., *11* 70-–5 1958)

Functional and cosmetic treatment of growth deficiencies of the upper face and related areas is a difficult one The dysplastic pattern of growth continues Even though the deformity may not be progressive it is not self-correcting and *there is no way to compensate for lost or* retarded growth Orthodontic prosthetic and surgical procedures give functional and cosmetic improvement The surgical procedures commonly used are directed toward contributing bulk and altering malposition. Osteotomy with or without a bone graft, and bone cartilage or alloplastic materials as a masking procedure, have been utilized Certain aspects *of treatment may be undertaken when the* patient is still growing but the final result cannot be attained until growth of the face has ceased

VII Summary and Conclusions

A series of surgical experiments on the septovomeral region of young growing and adult rabbits is reviewed and summarized The purpose was to relate this information to basic concepts of growth of bones and to possible clinical significance

After resection of the septovomeral region and/or large amounts of only cartilaginous *nasal septum in young growing rabbits there* was, as early as 4 days postoperatively a deceleration of growth of the snout a reversal of the incisal relationship and an overeruption of the incisors At post mortem in the experimental animals as contrasted with the controls, the snout was shorter and smaller with a resulting severe relative mandibular prognathism. The nasal and premaxillary bones were smaller as were the nasal cavity and piriform aperture At the posterior border of the septal defect there was a marked downward deflection of the nasal bones in an anterior direction This was in contrast to the smoothly curved dorsum of the control animals The extent and severity of the deformity varied approximately *with the amount of cartilaginous nasal septum* resected, the age of the animal at the time of resection and the length of the postoperative survival It is concluded that after resection the remaining cartilaginous nasal septum is unable to attain its full expression of growth The relationship of the cartilaginous nasal septum to growth of the snout can be compared with

that of the orbital contents to the growth of the orbit and the brain to the growth of the neurocranium.

When lesser amounts of cartilaginous nasal septum were resected (linear horizontal segments), the snout and dental deformities were also less pronounced. After temporary lateral dislocation of the cartilaginous nasal septum neither snout nor dental abnormalities were noted. All of the above were done in young rabbits. When large amounts of cartilaginous nasal septum were resected in adult rabbits, neither snout nor dental changes were observed.

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SUPPLEMENTUM 266

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BY

T LUNDBORG and S. LINZANDER

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The otomicroscopic observation and its clinical application

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I GENERAL VIEWPOINTS
INTRODUCTION

Before the era of chemoterapeutics and antibiotics the main interest of the otologist was focused on the healing processes of the diseased middle ear such as the character of the discharge and symptoms, indicating complications from adjacent structures. The condition of the middle ear was judged after inspection through an ordinary ear speculum or a Siegle's speculum. Modern ear microscopes were not available. For special investigation monocular microscopes had been constructed and used very early. These microscopes, however had many drawbacks and were never developed for routine clinical use. As a matter of fact, two Swedish otologists, C. O Nylén and G. Holmgren were among the initiators of otomicroscopy

The *International O.-R. L. Congress* in Amsterdam in 1953 was *important* for the development of modern reconstructive otosurgery because Zöllner and Wullstein presented their reports of pioneer work in this field, which led to increased activity all over the world. This new clinical activity was further based on the availability of chemoterapeutics and antibiotics as well as on modern otomicroscopes and new electro-acoustical hearing tests

CONTENTS

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The transmission mechanism is principally characterized by the following factors From the physical point of view the drum and ossicular chain are acting as a transformer of sound pressure during the collection and conduction of sound. The efficiency of this mechanism is determined by the relation between the acoustically active surface of the drum and the surface of the oval window with an additional lever mechanism of the ossicular chain This effect has been determined among others by Békésy and for frequencies under 2000 Hz it lies in the 25—30 dB level. In relation to the round window membrane the normal drum has a dampening and phase changing action, *the sound protection*. Small perforations of the drum, particularly when they are situated in the anterior parts and when the ossicular chain is normal, influence the hearing threshold very little because the sound pressure transformation still is good. When there are perforations in the posterior parts of the drum and when *the ossicular chain* is not intact, the sound pressure difference between the labyrinth windows is reduced as well as the normal difference in phase between the sound waves reaching the oval window and the round window Thus a cancellation of the normal sound protection may result in a hearing loss of the same size as the loss of the sound pressure transformer i.e. 25—30 dB In cases with subtotal drum perforation and loss of the ossicular chain both labyrinth windows are exposed to the sound waves. Such patients are clinically defined as "window hearers (Zöllner) According to the above mentioned factors the hearing loss in such cases lies in the 50—60 dB level In a series of 19 cases of chronic otitis of this type the average hearing loss in the frequencies 250—500—1000 Hz was found to be ca 50 dB (Hjorth, Lundborg & Rösler) When the drum is intact, but the ossicular chain is interrupted in its continuity there is a loss of the sound pressure transformation (25—30 dB) and a reduction of the sound protection, which totally results in a hearing loss of ca 50—60 dB When the ossicular chain is fixed in its epitympanal portion ("fixed malleus syndrome Goodhill) or when the stapedial footplate is fixed in the oval window (otosclerosis, tympanosclerosis) it may result in an audiometrically similar transmission hearing loss.

One has tried to define different types of transmission loss according to estimated changes concerning the mass, stiffnes and elasticity of the transmission system, when this is influenced by different types of pathology

These aims to classify various types of transmission loss from the physical point of view and evaluate the different physical factors, so far do not seem to have had any clinical importance.

PATHOLOGY

The chronic otitis, as is well known, has a complex pathological-anatomical basis, which is characterized by several dimensions. Different *phases* of the disease can be distinguished a) healed processes 2) latent inflammatory reactions and c) acute recurrences Individual cases reveal combinations of a), b) and c) From the *pathogenetic* point of view a) chronic otosalpingitis b) inflammation of the mucous membrane and c) osteitis can be considered.

Middle ear pathology is localized to the drum, the mucous membrane, the ossicles, the ligaments and muscles or the Eustachian tube The changes of the drum are constituted of changes in consistency forming, for instance, scars and of perforations. The scars appear either atrofic or hypertrofic by formation of new connective tissue, hyalinization, calcification or ossification. When there is a perforation, sometimes ephitelium is migrating over its margin on the promontorial wall. The middle ear mucosa can be changed in many ways, for instance hyperplasies, formation of cysts, granulations or ephitelial threads between and around the ossicles. When exsudative processes are organized or in

The technique of otoscopical examination had been further developed meanwhile and was also more widely used Earlier the aim of otoscopy was mainly topographical i.e to investigate pathological changes requiring removal by surgery Now the aim of otoscopy was more to establish a functional diagnosis with the emphasis on conservation to make reconstructive surgery possible

The Zeiss operation microscope for instance, has a system of prismas diminishing the convergence of the visual axes of the eyes, making stereoscopic observations through the external meatus possible This microscope also through another elaborate prismatic system illuminates the observed area completely Thus the meticulous observation of the tiny middle ear structures and also their manipulation with different instruments is greatly facilitated As a consequence of this development the use of otomicroscopy also was widened, including various diagnostic and therapeutic measures Without exaggeration it can be stated that modern otosurgery would be impossible without these microscopes. The functional approach in otomicroscopy has led to some direct tests of sound transmission "the remaining parts of the middle ear were also examined concerning their sound conduction properties (Zöllner)" for instance by the use of prosthesis tests, acoustic probe tests, Gellé-tests pneumophone test ad modum van Dishoeck, registration of stapedius reflex etc Each test has a different value in every individual case and therefore the combination of otomicroscopy and functional testing was described as "transmission testing" (Lundborg 1957) This type of transmission testing has to be completed with an evaluation of the tubar function and the cochlear function as well.

Experiences from various institutions during two decades of reconstructive otosurgery are quite different. Therefore the value of reconstructive otosurgery is debated One reason for that is probably the varying degree of exactness of the preoperative evaluation of each case in different case materials. Therefore these materials probably also constitute somewhat different conditions concerning the indications for reconstructive middle ear surgery

The improvement of hearing aids during this period has also made the treatment of deafness easier In the Scandinavian countries the resources for medical and social rehabilitation of patients with hearing loss have been raised through special audiological units and hearing centers, serving the ENT-clinics. A sociomedical legislation makes it possible to prescribe hearing aids and various accessories to hearing loss patients without costs to them

Thus the prescription of hearing aids is a further therapeutic possibility where reconstructive otosurgery is not chosen. Different opinions regarding the indications for surgery and also different degrees of surgical activity may influence the choice between the two therapeutical possibilities. In many cases it is necessary to use both methods Therefore those patient groups, which are referred preliminary either for otosurgical or electroacoustical treatment to a certain extent are identical This emphasizes the importance of close contact and cooperation between otological and audiological activities.

FUNCTION

During the last decades many details have been clarified concerning the function of both the normal and pathological middle ear Otosurgical and clinical-audiometrical methods and experiments on animals have been utilized. The sound transmission through the middle ear has been studied on series of experimental animals and also on the temporal bones from cadavers. Different types of drum perforations have been arranged as well as different kinds of obstacles, influencing the mobility of the drum and the ossicular chain Thus various clinical situations have been imitated and the corresponding hearing loss has been measured

The transmission mechanism is principally characterized by the following factors. From the physical point of view the drum and ossicular chain are acting as a transformer of sound pressure during the collection and conduction of sound. The efficiency of this mechanism is determined by the relation between the acoustically active surface of the drum and the surface of the oval window with an additional lever mechanism of the ossicular chain. This effect has been determined among others by Békésy and for frequencies under 2000 Hz it lies in the 25—30 dB level. In relation to the round window membrane the normal drum has a dampening and phase changing action, *the sound protection*. Small perforations of the drum, particularly when they are situated in the anterior parts and when the ossicular chain is normal, influence the hearing threshold very little, because the sound pressure transformation still is good. When there are perforations in the posterior parts of the drum, and when the ossicular chain is not intact, the sound pressure difference between the labyrinth windows is reduced as well as the normal difference in phase between the sound waves reaching the oval window and the round window. Thus a cancellation of the normal sound protection may result in a hearing loss of the same size as the loss of the sound pressure transformer i.e. 25—30 dB. In cases with subtotal drum perforation and loss of the ossicular chain both labyrinth windows are exposed to the sound waves. Such patients are clinically defined as "window hearers" (Zöllner). According to the above mentioned factors the hearing loss in such cases lies in the 50—60 dB level. In a series of 19 cases of chronic otitis of this type the average hearing loss in the frequencies 250—500—1000 Hz was found to be ca 50 dB (Hjorth, Lundborg & Rösler). When the drum is intact, but the ossicular chain is interrupted in its continuity there is a loss of the sound pressure transformation (25—30 dB) and a reduction of the sound protection, which totally results in a hearing loss of ca 50—60 dB. When the ossicular chain is fixed in its epitympanal portion ("fixed malleus syndrome" Goodhill) or when the stapedial footplate is fixed in the oval window (otosclerosis, tympanosclerosis) it may result in an audiometrically similar transmission hearing loss.

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Middle ear pathology is localised to the drum, the mucous membrane, the ossicles, the ligaments and muscles or the Eustachian tube. The changes of the drum are constituted of changes in consistency forming, for instance, scars and of perforations. The scars appear either atrophic or hypertrofic by formation of new connective tissue, hyalinization, calcification or ossification. When there is a perforation, sometimes epithelium is migrating over its margin on the promontoral wall. The middle ear mucosa can be changed in many ways, for instance hyperplasia, formation of cysts, granulations or epithelial threads between and around the ossicles. When exudative processes are organized or in

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The Zeiss operation microscope, for instance, has a system of prismas diminishing the convergence of the visual axes of the eyes, making stereoscopic observations through the external meatus possible This microscope also through another elaborate prismatic system illuminates the observed area completely Thus the meticulous observation of the tiny middle ear structures and also their manipulation with different instruments is greatly facilitated As a consequence of this development the use of otomicroscopy also was widened, including various diagnostic and therapeutic measures Without exaggeration it can be stated that modern otosurgery would be impossible without these microscopes. The functional approach in otomicroscopy has led to some direct tests of sound transmission the remaining parts of the middle ear were also examined concerning their sound conduction properties (Zöllner) for instance by the use of prosthesis tests, acoustic probe tests, Gellé tests, pneumophone test ad modum van Dishoeck registration of stapedius reflex etc Each test has a different value in every individual case and therefore the combination of otomicroscopy and functional testing was described as transmission testing" (Lundborg 1957) This type of transmission testing has to be completed with an evaluation of the tubar function and the cochlear function as well

Experiences from various institutions during two decades of reconstructive otosurgery are quite different. Therefore the value of reconstructive otosurgery is debated One reason for that is probably the varying degree of exactness of the preoperative evaluation of each case in different case materials Therefore these materials probably also constitute somewhat different conditions concerning the indications for reconstructive middle ear surgery

The improvement of hearing aids during this period has also made the treatment of deafness easier In the Scandinavian countries the resources for medical and social rehabilitation of patients with hearing loss have been raised through special audiological units and hearing centers, serving the ENT-clinics. A sociomedical legislation makes it possible to prescribe hearing aids and various accessories to hearing loss patients without costs to them

Thus the prescription of hearing aids is a further therapeutic possibility where reconstructive otosurgery is not chosen Different opinions regarding the indications for surgery and also different degrees of surgical activity may influence the choice between the two therapeutical possibilities In many cases it is necessary to use both methods Therefore those patient groups, which are referred preliminary either for otosurgical or electroacoustical treatment to a certain extent are identical This emphasizes the importance of close contact and cooperation between otological and audiological activities.

FUNCTION

During the last decades many details have been clarified concerning the function of both the normal and pathological middle ear Otosurgical and clinical-audiometrical methods and experiments on animals have been utilized The sound transmission through the middle ear has been studied on series of experimental animals and also on the temporal bones from cadavers. Different types of drum perforations have been arranged as well as different kinds of obstacles, influencing the mobility of the drum and the ossicular chain Thus various clinical situations have been imitated and the corresponding hearing loss has been measured

evaluated and discussed, one can state that, from the clinical point of view it does not seem fruitful to analyze, for instance, the sound pressure transformation, since this is a physical concept. As Kobrak emphasizes, it is almost impossible in diseased ears to assess the different physical factors of the sound conductive system as to their individual role in causing hearing loss. In connection with the otomicroscopic observation it seems more meaningful to state, how different pathology of the middle ear structures seems to influence *sound collection* and *sound conduction* which are the clinically comprehensible functions of the middle ear. Another essential component of the transmission mechanism—*sound protection*—is a well defined and accepted clinical concept.

1. *Chronic otitis with central perforation* with anatomically and functionally *intact ossicular chain*. Normal middle ear mucosa and functioning Eustachian tube. The hearing loss is depending on the size and position of the perforation *from 5—10* dB (small tubar perforations) to 20—30 dB (perforations in the posterior parts of drum, exposing the labyrinth windows). Indirect tympanoscopy with a 3 mm mirror may demonstrate the incudostapedial joint and the processus longus incudis intact and without surrounding inflammatory tissues (granulations, cholesteatoma etc.) See fig. 21—22—23 fig. 25—26, fig. 29—30

Covering prosthesis may compensate the hearing loss (closed gap in the audiogram), which demonstrates a functioning *ossicular* chain. Acoustic probe audiograms give via malleus an average transmission 20—25 *dB* better than via the promontory wall. The pathological changes in such a case influence mainly the *sound collection*. In such a "typical case" there is indication for myringoplasty which, as a rule, *shall* result in a closed gap and intact drum. The results are somewhat varying, depending on technique of operation, type of flap and the possibilities of postoperative, meticulous treatment and control. There are variations of this "typical case" for instance when the epithelium is migrating over the margin of perforation or when the middle ear mucosa shows "allergic reactions" for instance in the form of oedema, hypertrophy, adhesives etc. Changes of the tubar function and in the mastoid cellsystem—according to roentgenograms —of course have to be taken into consideration. Certain of these changes may contradict a myringoplasty.

See Case VII, VIII, IX

2. *Cronic otitis with central perforation and defective ossicular chain*. The hearing loss depends on the size and position of the perforation (30—60 dB)

Indirect tympanoscopy may show that the distal part of the processus longus incudis is defective, not reaching the stapes. Rather often the distal part of incus is *found* to be severed by an osteitic process but linked to the caput stapedis with threads of connective tissue. A prosthesis covering the perforation is not then resulting in an improvement of hearing, *but if* put in contact with the stapes, it may result in a substantial hearing gain. An acoustic probe audiogram gives, as a rule, 20—25 dB better transmission via stapes than via malleus and the promontory wall. The ossicular chain may reveal anatomical continuity but may be rigid at palpation with an ear probe. This results in reduced transmission properties, for instance when there is sclerosis in the attic, malleo-incudis *region*. (*Fixed malleus* syndrome, tympanosclerosis etc.) The perforation is reducing the *sound collection*, the changes in the ossicular chain reduce the *sound conduction* and often also the *sound protection* is reduced, when the labyrinth windows are exposed.

When the middle ear mucosa appears normal, without signs of cholesteatoma etc. and when the tubar function is normal, the drum perforation may be closed by a tympanoplasty which brings the drum in direct contact with

connection with ephitelial lesions, there are sometimes formed new connective tissue event ually with calcification In certain cases there are also ossification processes, for instance be-tween umbo and the promontory wall resulting in malleus fixation or in the round window niche, resulting in obliteration In epitympanum such formations may result in hard obliteration of the malleo-incudal articulation and its fixa tion to the attic wall (Fixed malleus syndrome" —Goodhill)

Similar formations may also appear in the oval window niche According to Zöllner and Beck this type of pathology is based on the combination of an ephitelial lesion and an aller gic reaction resulting in necrotisation lipoidiza tion and hyalinization of the connective tissue

Successively there may easily be a sedimen-tation of calcium salts Excessive reactions may result in a hard mass around the stapedial cru rae and even ossification of the annular liga ment (Paukensklerose") In the middle ear there may be a formation of new osteitic tissue —as a surplus formation—resulting from the irritation of the periost during long exsudative processes Thus, part of the ossicular chain may be transformed to masses, which can be diffi-cult to identify Osteitic processes appear in the ossicular chain during different periods of the chronic otitis, for instance in connection with cholesteatoma but also in connection with di rect trauma or pressure by foreign prosthesis materials Incus is most often affected by these processes According to Escher ca ⅔ of the osteitic processes are situated in the distal part of processus longus incudis

From the pathological-anatomical point of view each case requires an otomicroscopic exa mination in order to state if there is

a) a *central perforation* (and to inspect the middle ear mucosa the continuity of the os-sicular chain etc)

b) a marginal perforation (and thoroughly in vestigate if this seems to be an epitelized pouche in the attic region with clinical signs to be healed or if there are signs of active reactions with granulations, discharge cholesteatoma etc)

c) residuous chronic otitis, for instance with scars or collapsed parts of the drum, adhe sive to the promontory wall at some parts, eventually revealing reduced mobility at pal-pation etc *In these cases it is of particular* interest to notice otomicroscopically if the *tympanic membrane is movable during* Toynbees or Valsalvas tests, i.e if there is air passage from the tube to the labyrinth windows or if there are fibrous adhesives between the drum and the medial tympanic wall in a substantial part of the middle ear

Ingelstedt s and Flisberg s modification of Sieg-le s speculum using plain glass without magnifi-cation is a very useful otomicroscopical acces-sory It makes it easy to observe the mobility of different parts of the drum and malleus as well as the axis of the movements of malleus.

CLINIC

During the preoperative otomicroscopic exami nation and the evaluation of the middle ear function it is, of course necessary to study the transmission mechanism from pathological-ana tomical point of view as well as concerning the hearing to find an adequate basis for treatment and prognosis. When the isolated case is ex aminated such a variation is found both patho-logic anatomically and functionally that one can scarcely predict the indication for an otosurgial performance on the basis of a general know ledge of the transmission Inspite of these va riations and of the presence of clinical cases, which are on the whole very difficult to pene trate and evaluate, it is useful to mention some empirically found types of conductive deafness.

When the cases with conductive deafness are

II CLINICAL INVESTIGATIONS

THE ROLE OF OTOMICROSCOPY IN THE ASSESSMENT OF CONDUCTIVE DEAFNESS

To get a view as to what extent the otomicroscopy and various functional tests can be clinically utilized and evaluated, 100 cases of conductive deafness, consecutively admitted to the audiological unit for preoperative examination were studied. Cases of otosclerosis were not included, since the otoscopical findings, as a rule, are normal in these cases. (Lundborg, Linzander Lindström 1969.)

Tab 1 shows the case material, consisting of chronic otitis with central perforation, chronic otitis with marginal perforation, residue, adhesiv chronic otitis etc and how in the different groups of typecases the otomicroscopy and certain functional and audiometrical methods could be utilized in the evaluation of the conductive deafness cases. The number of cases examined in the different groups, of course, depends on to what extent different methods are applied, which explains the figures presented. The evaluation of these findings and test results have formed the basis for an indication of either myringoplasty tympanoplasty eventually together with a reconstruction of chain, "conservative atticoantrotomy etc. Explorative tympanotomy has been performed in conductive deafness cases without clear etiology to find out whether the ossicular chain is interrupted or defective for instance as a result of posttraumatic lesion or as a consequence of congenital malformation. In cases, where an operative indication was not considered, a hearing aid was prescribed according to normal rules

(The table possibly reflects a somewhat conservative surgical attitude compared with the conception of certain other clinical staffs.)

The survey demonstrates that otomicroscopy in relation to other examinations and tests was considered to be the most valuable element as a basis for diagnosis. The same tendency is reflected in the whole case material, on which this work is based (ca. 1000 cases)

Table 1 Transmission testing in 100 cases of chronic otitis etc and its clinical usefulness

	The evaluation based on					Indication for				
	Oto-micro-scopy	Indirect tympano-scopy	Proeth tests	Acoustic probe audio-grams	Other tests	Myringo-plasty	Tympano-plasty	Explora-tive tympano-tomy	Mastoid-ectomi etc.	No operation possibly hearing aid indi-cation
Central perfora-tion	48	18	39	41	—	30	1	2	12	3
Marginal perfora-tion	15	1	6	6	—	—	2	9	1	3
Residue	37		3	6	Gellé-test 18 pneumo-phone 10	—	—	2	22	13

stapes ("tympanostapediopexy") Stapes thus acts as a columella, substituting the rest of the ossicular chain In certain cases this results in a closed gap Tympanoplastics are technically performed in many different ways Many types of columellas are utilized and the results vary There are certain conditions, which sometimes contradict a tympanoplasty for instance excessive cholesteatoma, pronounced hyperplasy of the middle ear mucosa, adhesives in the tubar portion of the middle ear etc.

See Case X XI

3 *Chronic otitis with marginal perforation* Occasionally the hearing may be influenced very little by small perforations in the attic or central part of the drum in spite of excessive granulation and cholesteatoma around the ossicles. The primary task in such cases is to remove inflammatory tissues from the ear All such tissues, for instance osteitis, cholesteatoma etc have to be removed by an atticotomy "conservative" if possible In cholesteatoma cases one often has to resect caput mallei If a certain continuity of the ossicular chain thus may be conserved, there is occasionally a fairly good transmission and a clinical healing of the inflammatory processes In other cases incus has to be extracted The changes mainly influence *sound conduction* in these cases The earlier method of choice in connection with chronic otitis, when a radical cavity was created, to a certain extent can be substituted by the above mentioned more conservative performance.

See Case XII

4 *Chronic adhesive otitis* Often the drum is atrofic, collapsed and to various extent also adherent to the promontory wall The ossicular chain is rigid and sometimes defective, for instance by luxation of incudostapedial joint as a result of transudate organisation. The cause is often an impaired tubar function The conductive hearing loss varies, depending upon the degree of drum mobility etc The changes are mainly influencing *sound collection* and *sound conduction* Because of the bad tubar function and a pronounced tendency to form adhesives, it is often not possible in these cases to create a normal, "mobile" middle ear

See Case V VI

5 *Chronic residuous otitis with drum scars and defects of ossicular chain* There are cases like the end result of an inflammatory process in appearance which have a traumatic genesis. Direct violence towards the drum and ossicles can result in luxation or lesion of incus In connection with blows and pressure from the sides of the skull and also in connection with mastoidectomies, incus may be luxated in a similar way In such cases there may be a maximal conductive deafness (50—60 dB) because the changes are influencing *sound collection sound conduction* and *sound protection* as well If the drum (scar) is thin, the incus lesion may be diagnosed otomicroscopically There are functional tests giving additional information concerning possible ossicular chain defects Often a tympanotomy is indicated If processus longus incudis is defective but stapes is found anatomically normal and movable in the oval window at palpation, a tympanostapediopexy may reconstruct the transmission and give permanent results under certain conditions.

See Case IV

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THE CLINICAL APPLICATION
(Documentation and Discussion)

In order to give a medically well based service to those large groups of patients for whom—at the first examination—either otosurgery or hearing aid ordination seem adequate different institutions achieved various solutions concerning arrangements for the patients Because there is a considerable overlapping by these major patientgroups, this offers a certain problem of organisation According to the authors experience, gained during a number of years, this task can be fruitfully approached by the departments of otology and audiology in close cooperation. At regular staffmeetings the test results from the cases of the week are demonstrated and recommendations are made concerning otologic and audiologic measures. A clearly arranged statement of the performed examinations is necessary both from clinical and didactical point of view In connection with the otomicroscopy it is of particular value to illustrate the findings from drum and middle ear by sketches on stencilled patterns and by color photos of the otoscopic findings To gain time, surveyability and uniformity in the evaluation of cases, the findings of examination are presented in special journals, from which diapositives in the size of 70×70 mm easily are made, using a reproducting apparatus (Polaroid Copymaker) Within the frame of these slides, color copies in the size of 20×20 mm can be applied Magnified machine made paper copies in color are included in the journals

To get an uniformity in connection with the establishment of operative indication in cases with conductive deafness it has proved to be necessary to demonstrate and discuss continuously a large number of cases within the staff This further emphasizes the need of a documentation of the otoscopial findings together with the functional tests etc

A *photographic documentation* of the otoscopic findings is an ideal method for high-fidelity recording of current data because the demonstration simplifies the situation for all staff members Its availability for follow-up studies also offers practical advantages. These findings can be compared with functional tests in order to study the functional significance of various morphological findings The functional loss, caused by various pathologic changes in the drum, the ossicular chain, middle ear mucosa etc is often not clearly understood

At the examination of the individual case and during the *observation* of pathologically changed middle ear structures, in our discussions one has tried to compare those findings with the audiograms and other functional tests. It seems clinically meaningful—as is already *mentioned— to evaluate simultaneously which* of the clinically comprehensible elements of the conductive mechanism —i.e the *sound collection* the *sound conduction* and the *sound protection*—that are pathologically changed, requiring correction

Because essential physiological knowledge concerning the normal as well as the diseased conductive mechanism has been gained clinically by means of preoperative examinations, otosclerosis surgery reconstructive otosurgery in cases with chronic otitis etc it seems *fruitful* to continue this work, following a clinical conception by *critical observations of human physiopathology*" (V Goodhill) For a number of years the oto-audiological team has been working in accordance with the approach sketched above (observation, documentation and discussion) This, as we believe has been a positive experience and therefore a brief survey may be of some interest

THE OTOMICROSCOPICAL EQUIPMENT AND PHOTOTECHNIQUE

Making photos with the original types of otomicroscopes offered many difficulties and pictures of acceptable quality were rare Long ex

posure times were required with the light sources and films available and the pictures became unsharp, because the patient did not remain still. Further it was not possible to choose a diaphragme aperture small enough to get sufficient depth of field. Elaborate otomicroscopical systems were developed by Schultz van Treeck (194?), Kobrak (1956) and others, but only for special laboratory conditions and special purposes, not for clinical routine work.

Principally the authors aim was to take photos during the ordinary otomicroscopic examination in order to develop *a routine technique used as a standard clinical performance*. Therefore a modern stereoscopic otomicroscope with light supply through the lens system was the first prerequisite.

Attempts to take black & white pictures with a Polaroid camera applied on one of the oculars of a Zeiss microscope, only occasionally gave usable results and with the sacrifice of binocular orientation.

The film is very sensitive (A.S.A. = 3000) but pictures were *found to be of too little contrast*, which made the observation of fine structures difficult.

The next step in order to get more informative pictures was to try color photography. Polaroid Color Film, however, is too unsensitive (A.S.A. = 75) and satisfactory results were not obtained with that film.

Thus a color film of sufficient sensitivity was another prerequisite. Kodak High Speed Ektachrome Type B color reversal film (E.A.B = 135—20) was found to be suitable (A.S.A. = 125).

The commercially available "Beam splitter" (Code 301513) and "Photoadapter" (Code 30151?) constituted important accessories for the application of cameras on a Zeiss operation microscope. The light supply of the ordinary equipment however, with its 50 W lamp, as a rule offered insufficient illumination through the ear speculum on the drum and middle ear structures.

Therefore some *new constructions* had to be made.

1. The ordinary lamp was replaced by a halogen projection lamp of 250 W.

2. This lamp was put in a new lamphouse, equipped with a spherical mirror.

3. A device making it possible to overvoltage the lamp during a very short moment (29 V 1/10 sec.). By means of another device a synchronized impulse is given to an electrically conducted shutter resulting in maximal illumination only during the required exposure time.

4. A cooling fan for the lamphouse.

5. The ear speculas were painted grey to resemble the reflex conditions of the skin. This was done to facilitate the machine copying. A speculum with very high (shiny) or very low (black) reflection will give too high light contrast for the copying machine to handle. The colored paper copies are not, as a rule, of the same quality as the diapositives, but they are useful in the journals etc.

The Contarex S camera housing offers the possibility *to apply a special identification strip* for each patient. The strip is put in the camera *in direct contact with the film*, and the patients initials etc. written upon it will be copied in each film.

In order to raise the quality of the photography further trials are being made with electronic flashlight. The problem in this connection is to get the light into the condenser system.

Especially for photography during operation a motordriven filmtransport in the camera would be convenient.

With the present equipment an exposure time of 1/30sec. and a diaphragme aperture at the photoadapter of 1/22 are chosen. Using these

values one is getting acceptable results i terms of exposure, depth of field and freedom from unsharpness due to movements of the patient. Further development of the method however will make it possible to use a shorter exposure time, say 1/125 sec., and a smaller aperture say 1/64 which above all would make the procedure easier and give better results in the hands of photographically unexperienced examiners.

Standard accessories

(A) Small beam splitter (Code 301513)
(B) Large observation tube (Code 305143)
(C) Photoadapter (Code 301512)
(D) Standard Contarex S camera Housing with identification strip Alternatively (E) Siemens TV-camera, (F) Beaulieu Film-Camera

V ·rking distance 20 cm
Magnification 16 (at the ocular)

Special accessories

(G) 24 V 250 V Philips halogen projection lamp with
(H) A new lamphouse including fan and
(J) a device for momentaneous over voltage of the lamp (Max ca 29 V)
(K) Ear speculas painted grey
(L) Siegle s speculum (a.m Ingelstedt—Filesberg)

Film Kodak High Speed Ektachrome Type B color reversal film (EHB 135—20)

Exposure time 1/30 sec.
Diaphragme aperture f 22

Color-copies 9 × 12 cm (routine-made by commercial color laboratory)
Cost pro examination 3 *US $*

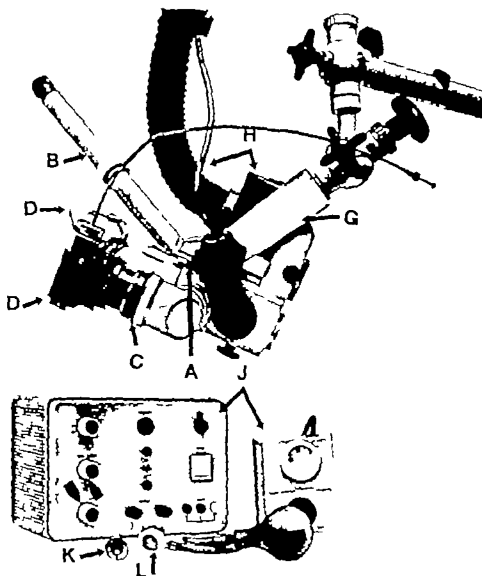


Fig. 1. Equipment for Otomicroscopy and Photography. Zeiss op.-microscope with standard and special accessories.

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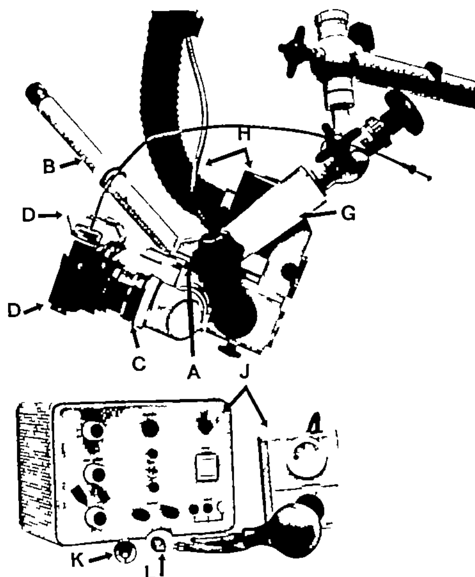


Fig. 1. Equipment for Otomicroscopy and Photography. Zeiss op.-microscope with standard and special accessories.

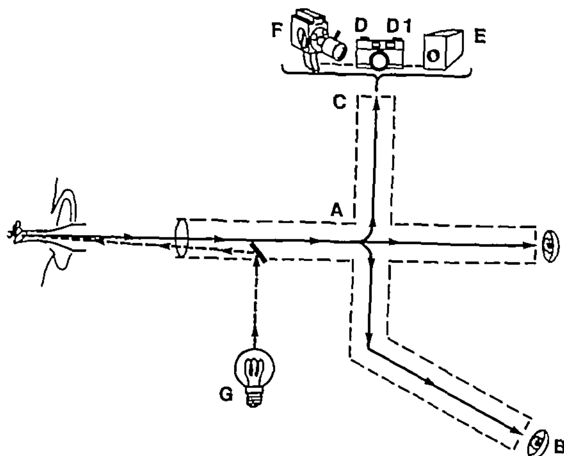


Fig 2 Semischematic sketch of the Equipment in fig. 1

CLINICAL CASE EXAMPLES

Otomicroscopic findings and function
A series of cases with warying middle ear pathology documented by 4-color pictures and corresponding halfshema tic black and white sketches with in dication of relevant anatomical land marks will be presented (See legend) The otoscopic observations are com pared with audiograms and other clini cal and functional investigations In connection with the discussion of diag-nosis and prognosis an evaluation is also made about how the different pa thologic changes seem to influence the clinically comprehensible elements of conductive mechanism i e sound col lection sound conduction sound pro-tection

Legend of indicated anatomical structures

1 Processus brevis mallei
1B Rest of manubrium mallei
2 Umbo (membranae tympani)
3 Promontorium
3a. Fenestra rotunda
4 Articulatio incudostapedia
Caput stapedis
5 Crus post. stapedis
6 Tendo m. stapedii
7 Processus longus incudis
8 Corpus incudis
Processus brevis incudis
9 Chorda tympani
10 Lig. mallei post
11 Cholesteatoma of the attic region
12. Articulatio malleoincudis
13 Limbus membranae tympani



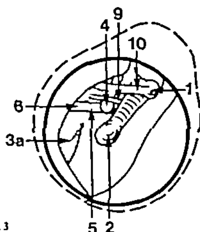
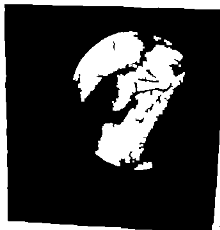


Fig. 3



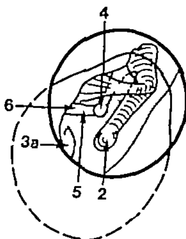


Fig. 4

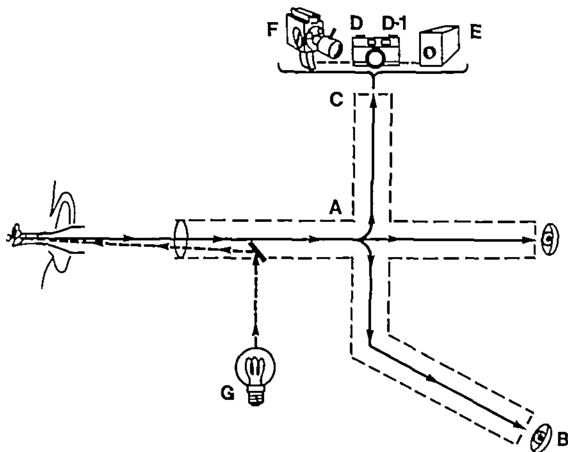


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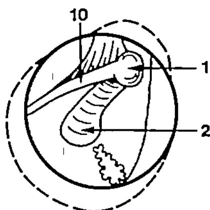


Fig. 7



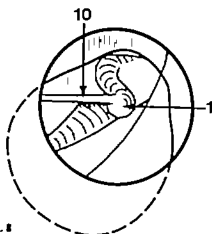


Fig. 8

Fig. 7. Fig. 8. Right ear. Normal tympanic membrane with moderate transparency



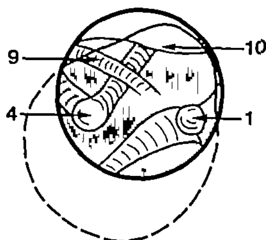


Fig 5



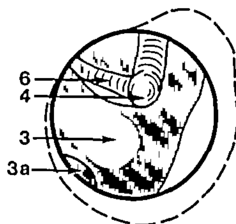


Fig 6

Fig 3 Fig 4 Fig 5 Fig 6 Right ear Normal tympanic membrane with pronounced transparency Proc. brevis mallei and lig mallei post limits the smaller epitympanic part of the drum, pars flaccida against the major part pars tensa, where threads can be seen In the upper posterior quadrant the dark oval window niche where processu longus incudis is apparent with articulatio incudostapedia. In the lower posterior quadrant the dark round window niche

Fig 4 Fig 4 Survey of tympanic membrane

Fig 5 Fig 6 Shows the al window niche (5) and the round w w he (6)

Fig 5 Sho ld be t ned 90 in the anticlock wise direct on



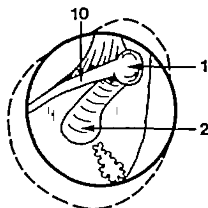


Fig. 7



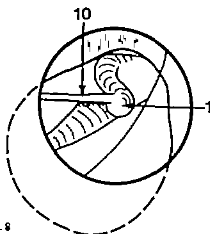
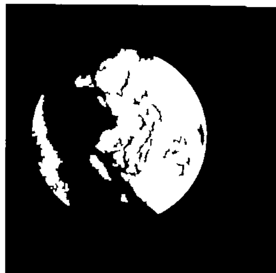


Fig. 8

Fig. 7, Fig. 8. Right ear. Normal tympanic membrane with moderate transparency.



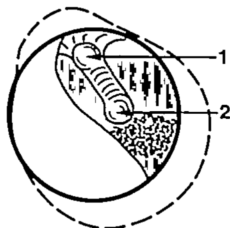
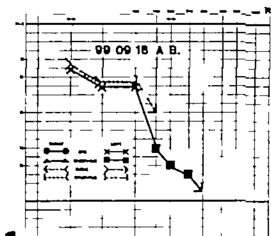
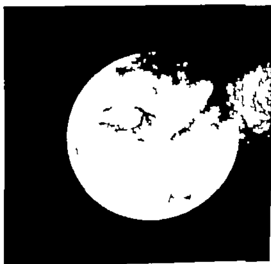


Fig. 9



Audiogram Case I.

Fig 9 Case I (99-09-18 A.B.)
Left ear RESIDUOUS TYMPANIC MEMBRANE.
Sensori-neural deafness. Transmission normal. Audiogram with no gap between air conduction and bone conduction. Tympanic membrane not transparent, atrofic in the upper parts, thickened and with calcification in the lower parts, freely movable.
The central arterial network appears along malleus.
Post inflammatory cochlear lesion probable



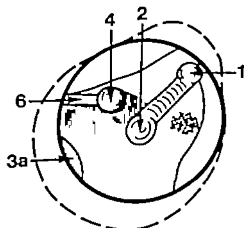
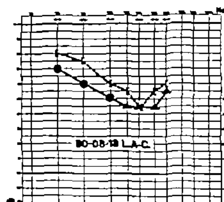


Fig. 10



Audiogram Case II.

Fig. 10 Case II (50-08-18 L.A.—C)
Right ear COMBINED DEAFNESS. Residue after chronic otitis.
Larger part of pars tensa atrofic, partly with calcification. Tympano-stapediopexy (adhesions between tympanic membrane and articulatio incudostapedia).
Gap: ca 10 dB. The changes within the middle ear influence both sound collection and sound conduction.



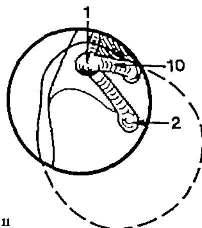


Fig. 11



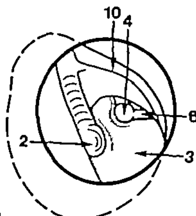


Fig. 12



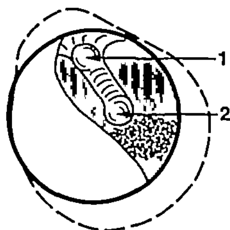
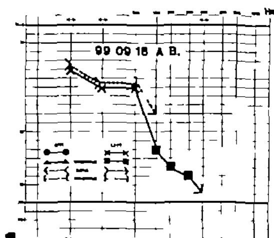


Fig. 9



Audiogram Case I.

Fig 9 Case 1 (99-09-18 A.B.)
Left ear RESIDUOUS TYMPANIC MEMBRANE.
Sensori-neural deafness. Transmission normal. Audiogram with no gap between air conduction and bone conduction. Tympanic membrane not transparent, atrofic in the upper parts, thickened and with calcification in the lower parts, freely movable.
The central arterial network appears along malleus.
Post inflammatory cochlear lesion probable.



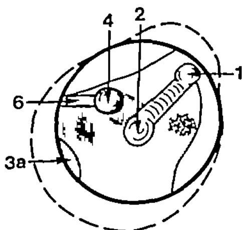


Fig. 10



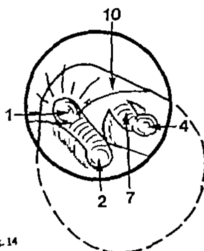
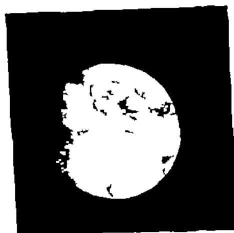


Fig. 14



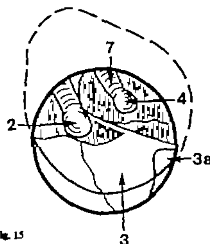


Fig. 15



Audiogram. Case V

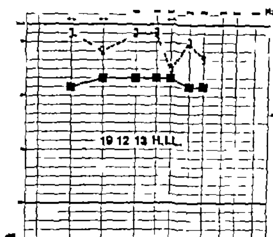
Fig. 14 Fig. 15 Case V (12 13-15 C.N.)
OTIT. MED. CHRON. ADHESIV. SIN.

Tympanic membrane totally retracted, adherent to the promontory wall and articulatio incudostapedia.

Malleus reveals reduced mobility at palpation, stapes mobile.

Gap: 10—15 dB. The changes influence sound collection and sound conduction. Transmission by means of tympanostapediopexy (adhesions between tympanic membrane and stapes).

Therapy: Doubtful indication for operative performance.



Audiogram Case III

Fig 11 Fig 12 Case III (19-12 13 *H L—L*)
OTIT MED CHRON RESID SIN
Tympanic membrane partly atrofic (scars) after earlier perforation. Ossicular chain retracted and rigid at palpation, sclerotic changes in the articulatio malleoincudis region as inflammatory sequelae.
Gap. 20 dB The changes influence *mainly* sound conduction Fixed malleus *syndrome*
Therapy Exploration of the attic *part of the* ossicular chain.



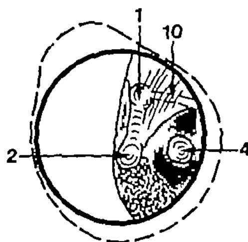
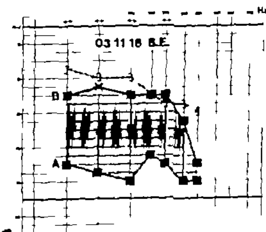


Fig. 13



Audiogram. C se I
Preoperative conduction (A) Postoperative air condu t on (B).

Fig 13 Case IV (03 11 18 S.E.)
OTIT MED CHRON RESID POST TRAUMATICA SIN Necrosis proc longus incudis sin
Residuous tympanic membrane with *a thin* scar in the upper posterior quadrant Processus longus incudis *not* visible
Gap 50 dB Interruption of the ossicular chain no sound collection, no sound conduction and no sound protection.
Therapy Tympanotomy reveals necrosis of processus longus incudis Tympanostapediopexy restores transmission (Postoperative air conduction level [B] in audiogram)



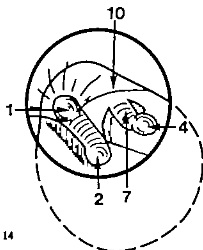


Fig. 14



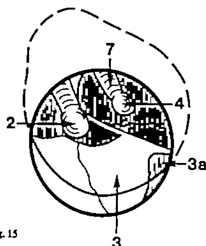
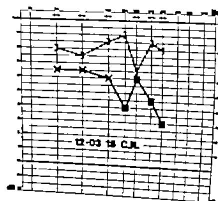


Fig. 15



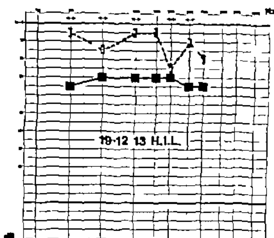
Audiogram. Case V

Fig 14 Fig 15 Case V (12 13-15 C.N.)
OTIT MED CHRON. ADHESIV SIN.
Tympanic membrane totally retracted, adherent to the promontory wall and articulatio incudostapedia.

Malleus reveals reduced mobility at palpation, stapes mobile.

Gap: 10—15 dB. The changes influence sound collection and sound conduction. Transmission by means of tympanostapediopexy (adhesions between tympanic membrane and stapes).

Therapy: Doubtful indication for operative performance.



Audiogram Case III

Fig 11 Fig 12 Case III (19-1 13 H.I.—L)
OTIT MED CHRON RESID. SIN
Tympanic membrane partly atrofic (scars) after earlier perforation Ossicular chain re tracted and rigid at palpation, sclerotic changes in the articulatio malleoincudis re gion as inflammatory sequelae
Gap 20 dB. The changes influence *mainly* sound conduction. Fixed malleus syndrome
Therapy Exploration of the attic part of the ossicular chain



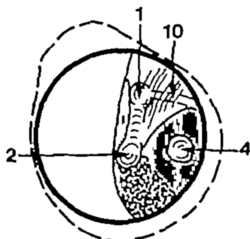
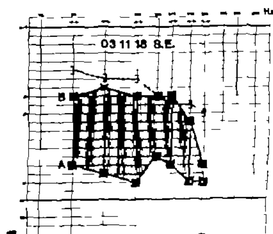


Fig. 13



Audiogram. Case IV
Preoperative air conduction (A). Postopera ti e air conduction (B).

Fig 13 Case IV (03-11 18 S E.)
OTIT MED CHRON RESID POST TRAUMATICA SIN Necrosis proc. longus incudis sin.
Residuous tympanic membrane with a thin scar in the upper posterior quadrant. Proces sus longus incudis *not* visible.
Gap 50 dB Interruption of the ossicular chain, no sound collection, no sound conduc tion and no sound protection.
Therapy Tympanotomy *reveals necrosis of* processus longus incudis. Tympanostapedio-pexy restores transmission. (Postoperative air conduction level [B] in audiogram)

INDIRECT TYMPANOSCOPY

Fig 18 Fig 19 Fig 20 Fig 21 Fig 22 Fig 23 Case VII (32 12-09 V V)

Fig 18 Fig 19 Ear speculum towards upper (18) and lower (19) parts of tympanic membrane.

Fig 20 Head of patient flected in contralateral direction for visualisation of articulatio incudostapedia.

Fig 21 Fig 22 Fig 23 Intratympanal mirror of 3 mm ø in three different positions for visualisation of distal, middle and proximal parts of incus.





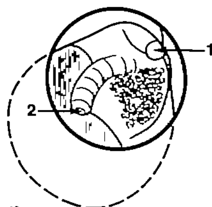


Fig 18



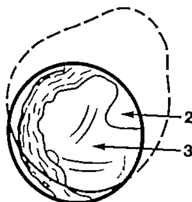
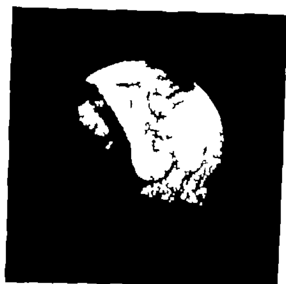


Fig. 19



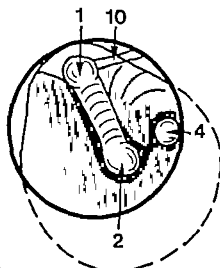


Fig. 16



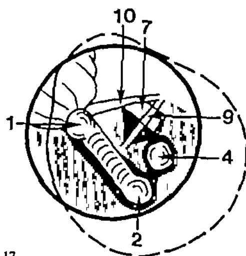
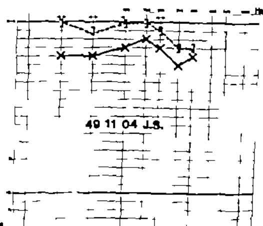


Fig. 17



Audiogram Case VI

Fig 16 Fig 17 Case VI (49-11-04 J.S.)
OTIT MED CHRON ADHESIV SIN
Tympanic membrane totally retracted with adhesions to the promontory wall.
Malleus rigid at palpation, stapes partly movable
Loss of processus longus incudis.
Gap: 20 dB The acoustically active surface of the tympanic membrane consists of a small air filled part around stapes. Changes in fluence sound collection and sound conduction.
Therapy: Doubtful indication for operative performance



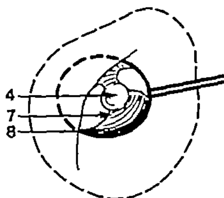
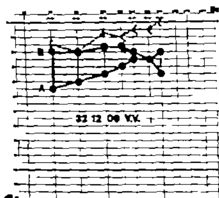


Fig. 23



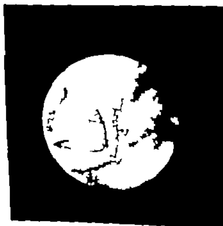
Audiogram. Case VII.
A. Air conduction without prosthesis.
B. Air conduction with covering prosthesis.

OTIT MED. CHRON C. PERF CENTR. DXT

Central perforation of the tympanic membrane with normal middle ear. Both oval window and round window niches mainly protected against sound. Indirect tympanoscopy by means of mirror reveals the ossicular chain anatomically intact.

Gap: 20—25 dB. Covering prosthesis fitted over the perforation results in closed gap. The ossicular chain functioning. The changes influence mainly sound collection.

Therapy: Typical case for myringoplasty



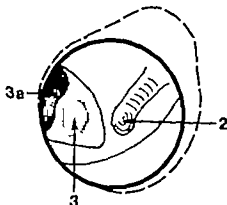
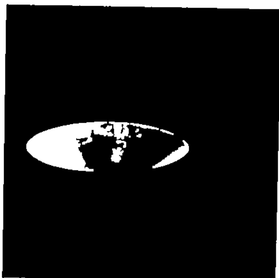


Fig. 24



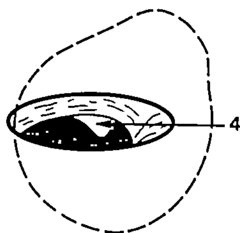


Fig. 20



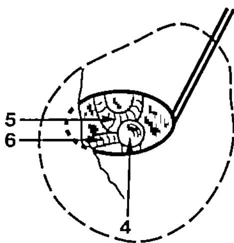
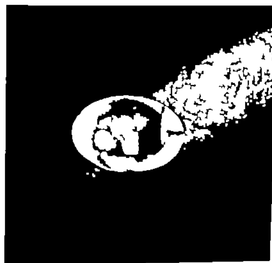


Fig. 21



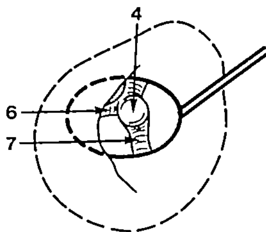


Fig. 22



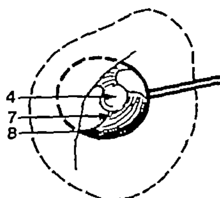
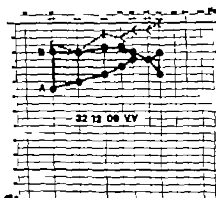


Fig. 23



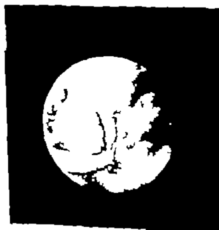
Audiogram. Case VII.
A. Air conduction without prosthesis.
B. Air conduction with covering prosthesis.

OTIT MED. CHRON C. PERF CENTR. DXT

Central perforation of the tympanic membrane with normal middle ear. Both oval window and round window niches mainly protected against sound. Indirect tympanoscopy by means of mirror reveals the ossicular chain anatomically intact.

Gap: 20—25 dB. Covering prosthesis fitted over the perforation results in closed gap. The ossicular chain functioning. The changes influence mainly sound collection.

Therapy: Typical case for myringoplasty



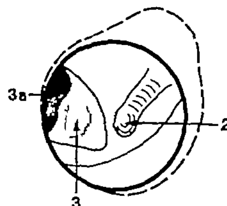


Fig. 24



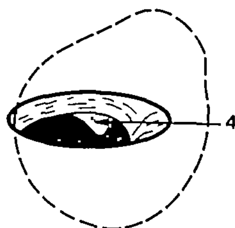


Fig. 20



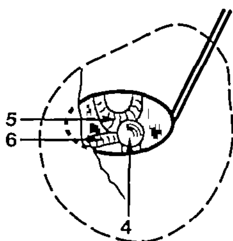
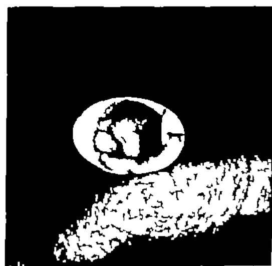


Fig. 21



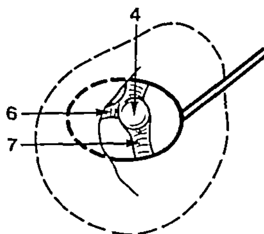


Fig. 22



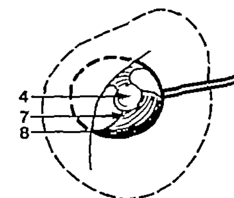
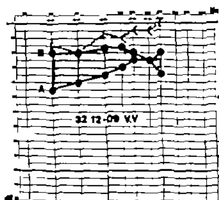


Fig. 23



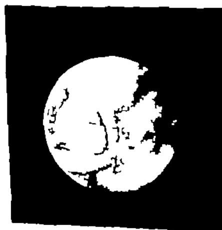
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Therapy: Typical case for myringoplasty



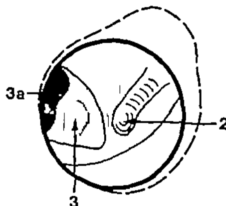
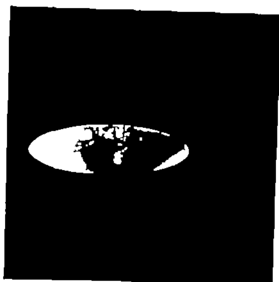


Fig. 24



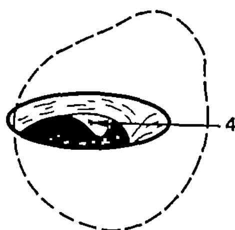


Fig. 20



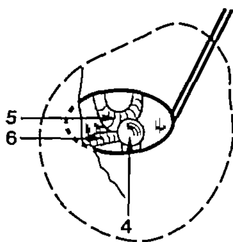


Fig. 21



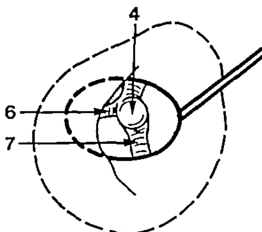


Fig. 22



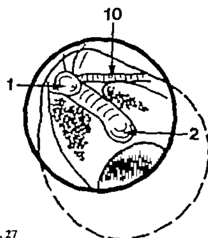


Fig. 27



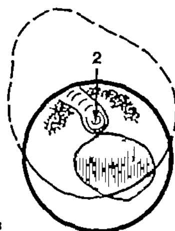


Fig. 28



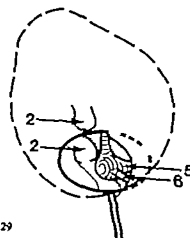


Fig. 29



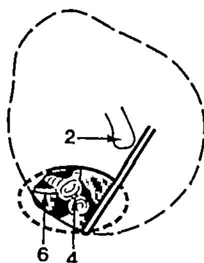


Fig. 25



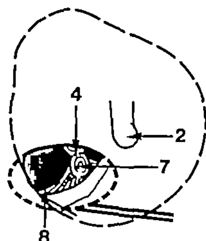
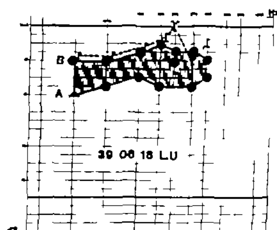


Fig. 26



Audiogram Case VIII

A Air conduction without prosthesis

B Air conduction with covering prosthesis

Fig 24 Fig 25 Fig 26

Case VIII (39-09-18) L.U)

OTIT MED CHRON C. PERF CENTR DXT

Central perforation of the tympanic membrane with normal middle ear Round window niche exposed. Ossicular chain anatomically intact Almost identical conditions with Case VII

Gap. 20—25 dB Gap closed by covering prosthesis. Ossicular chain functioning (Sound collection reduced).

Therapy Typical case for myringoplasty



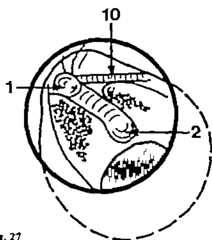


Fig. 27



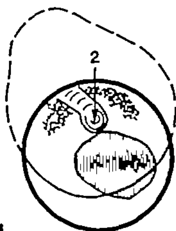


Fig. 28



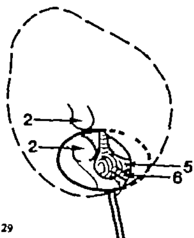


Fig. 29



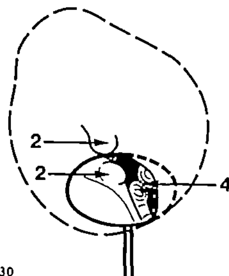
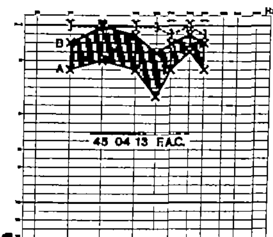


Fig. 30



Audiogram. Case IX
A. Air conduction without prosthesis.
B Air conduction with covering prosthesis.

Fig 27 Fig 28 Fig 29 Fig 30
Case IX (45-04-13)
OTIT MED CHRON C. PERF CENTR. SIN
Central tympanic membrane with normal middle ear Ossicular chain anatomically intact. (See Case VII, Case VIII.)
Gap 20—25 dB. Gap closed by covering prosthesis. Ossicular chain functioning (Sound collection reduced).
Therapy Typical case for myringoplasty



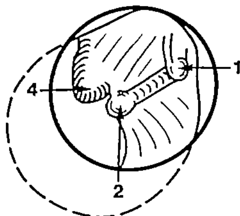


Fig. 31



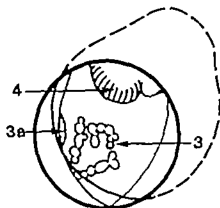
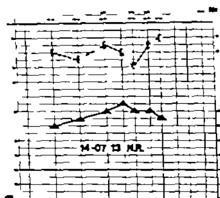


Fig. 32



Audiogram. Case X.

Fig 31 Fig 32 Case X (14-07 13 N.R.)
OTIT MED CHRON. C. PERF CENTR. C. TYMPANOSCLEROSIS DXT

Fibrotic tympanic membrane with central perforation and normal middle ear revealing spiculae on promontory wall. Articulatio in cudostapedia thickened, deformed and rigid at palpation (Tympanosclerosis).

Gap: 40—50 dB. Application of moist cotton prosthesis on stapes without effect. Ossicular chain not functioning. The changes reduce sound collection, sound conduction and sound protection as well.

Therapy: Exploration of ossicular chain, removal of sclerotic tissue, inclusive stapediolysis.



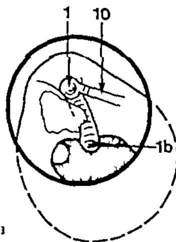


Fig. 33



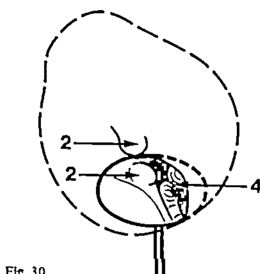
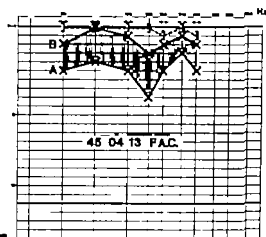


Fig. 30



Audiogram Case IX
A. Air conduction without prosthesis.
B Air conduction with covering prosthesis.

Fig 27 Fig 28 Fig 29 Fig 30
Case IX (45-04-13)
OTIT MED CHRON C. PERF CENTR. SIN
Central tympanic membrane with normal middle ear Ossicular chain anatomically intact. (See Case VII Case VIII.)
Gap 20—25 dB Gap closed by covering prosthesis. Ossicular chain functioning (Sound collection reduced).
Therapy Typical case for myringoplasty



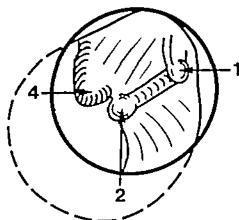


Fig. 31



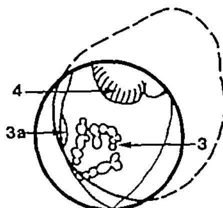
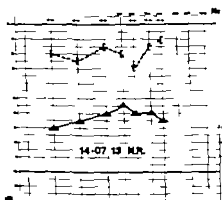


Fig. 32



Audiogram Case X.

Fig 31 Fig 32 Case X (14-07 13 N.R.)
OTIT MED CHRON C. PERF CENTR. C. TYMPANOSCLEROSIS DXT
Fibrotic tympanic membrane with central perforation and normal middle ear revealing spiculae on promontory wall. Articulatio in cudostapedia thickened, deformed and rigid at palpation (Tympanosclerosis).
Gap: 40—50 dB. Application of moist cotton prosthesis on stapes without effect. Ossicular chain not functioning. The changes reduce sound collection, sound conduction and sound protection as well.
Therapy: Exploration of ossicular chain, removal of sclerotic tissue, inclusive stapediolysis



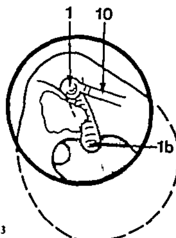


Fig. 33



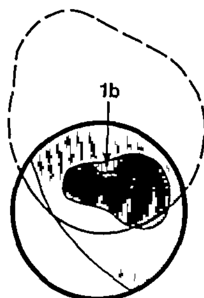


Fig. 34



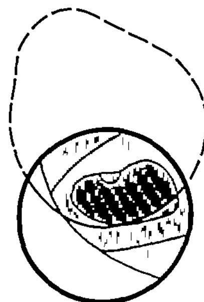
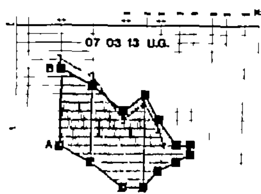


Fig. 35



Aud og ... XI
A A... duct ... without prosthesis.
B Ai... uct... with st... pes prosthesis.

Fig 33 Fig 34 Fig 35
Case XI (07-03 13 U G)
OTIT MED CHRON C PERF CENTR SIN
Fibrotic tympanic membrane with central perforation and pathologic tissue in the middle ear *Malleus rigid at palpation. Ad*hesions around articulatio incudostapedia (interruption of chain?).
Gap 45—50 dB Covering prosthesis without effect Prosthesi applied on stapes closes the gap
The changes reduce sound collection, sound conduction and sound protection as well
Therapy Reconstruction of the middle ear with tympanoplasty



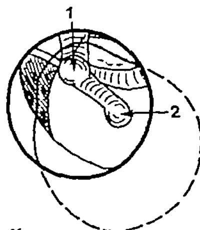


Fig. 36



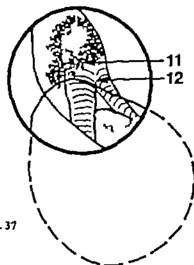
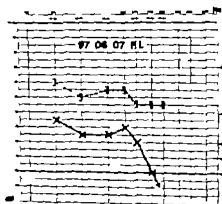


Fig. 37

Fig 36 Fig 37 Case XII (97-06-07 F.J.)
OTIT. MED. CHRON. C. PERF. ATTIC.
ET CHOLESTEATOMA SIN.
Fibrotic tympanic membrane intact in pars tensa. Attic perforation with cholesteatoma and osteitis. Sclerotic tissue around articulatio malleoincudis.
Gap 25 dB. Sound conduction reduced by granulative tissue around malleus and incus.
Therapy: Atticotomy



Audiogram: Case XII.



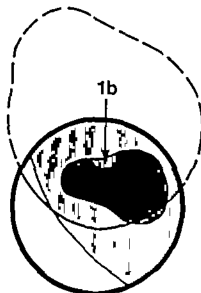


Fig. 34

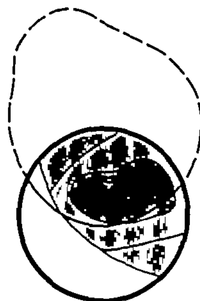
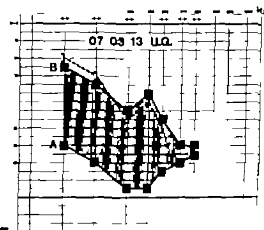


Fig. 35



Audiogram. Case XI
A Air conduction w th p osthesis
B Air cond tion w th stapes prosthesis

Fig 33 Fig 34 Fig 35
Case XI (07-03 13 U G)
OTIT MED CHRON C PERF CENTR SIN
Fibrotic tympanic membrane with central perforation and pathologic tissue in the middle ear Malleus rigid at palpation. Ad hesions around articulatio incudostapedia (interruption of chain?).
Gap 45—50 dB Covering prosthesis without effect Prosthesis applied on stapes closes the gap
The changes reduce sound collection, sound conduction and sound protection as well
Therapy Reconstruction of the middle ear w th tympanoplasty

III GENERAL DISCUSSION AND CONCLUSIONS

THE ACTUALITY OF MIDDLE EAR PROBLEMS

Activities in otology and audiology during the last decades have greatly contributed to the understanding of the function of hearing and of the diagnosis and therapy of deafness.

The clinical work and research within this field are reflected, for instance, in scientific journals and international congress programs. The interest is apparently more focused at *cochlear than middle ear problems* as it can be seen, for instance, in D.S.H.—Abstracts (Deafness Speech and Hearing Publications) Archives of Otolaryngology and in Berendes—Link Zöllners Handbook, which probably constitute some of the most representative surveys of the fields of interest.

Thus, formulation of questions providing incentives to investigate problems concerning the cochlea seem to have been fruitful. Utilizing different scientific methods (electronmicroscopy electrophysiology cytochemistry microanalysis etc.) many important details of the inner ear's morphology and function have been clarified.

The conditions are not quite the same concerning the middle ear. There have been presented many contributions having clarified the middle ear function and there are positive—sometimes excellent—results from the treatment of different types of conductive deafness. Despite of this many reports and discussions reflect a certain disappointment concerning several parts of otosurgery the possibilities of evaluating the function of the Eustachian tube etc. From the clinical point of view of course, these obstacles and hesitation have to be overcome.

One reason for this attitude seems to be a discrepancy between the clinical activities and the non-otologic activities using physical and physiological concepts and their application to the problems of the sound conduction mechanism. Clinicians cannot be expected to consider testresults etc., if these are relating purely physical concepts, often formulated in terms, which are not clearly understood from the clinical point of view.

On the other hand, otology and audiology have revealed clinical evidence of therapeutic measures, which cannot always be clearly interpreted on physical grounds. Such situations should reasonably—with satisfactory cooperation—act as a challenge to research in the theoretical disciplines.

Thus—when an evaluation is made to correlate the observation of middle ear pathology and the hearing loss, expressed in terms of various functional tests—it seems convenient to use clinically comprehensible factors concerning the conductive mechanism and middle ear.

There is clinical evidence from the observations of many individual cases with hearing loss, that these factors, for instance, show great quantitative variations. A case with central drum perforation may according to preoperative evaluation, have a prognosis of 25 dB hearing gain, but the myringoplasty can result in an improvement of 45 dB. On the basis of this examination one can predict the result to be within some kind of level-interval but sufficient exactness is not yet achieved. Therefore many aspects of the sound conduction mechanism under both normal and pathological conditions have to be clarified.

This knowledge seems to be gained by an otomicroscopical approach and investigations of clinical case materials with different types of sound-conductive deafness.

Increased clinical activities with the middle ear

Because of the many functional, diagnostic and therapeutic problems from the middle ear one can expect increased clinical activities dealing with the middle ear and the conductive deafness due to causes arising here.

The case materials with conductive deafness which need investigation and treatment are also



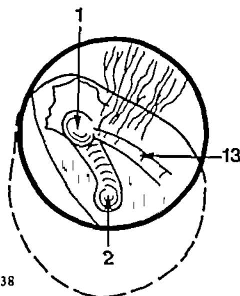
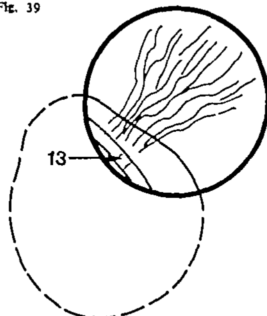
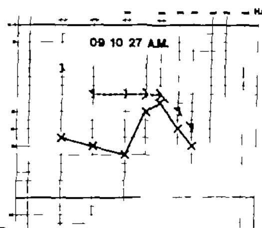


Fig. 38

Fig. 39







Audiogram Case XIII

Fig 38 Fig 39 Case XIII (09-10-27 A M)
ST POST FENESTR. A. M LEMPERT SIN
Radical cavity left ear with normal epitelization. Tympanic membrane normal. Caput mallei resected Incus extracted Sourdille-flap

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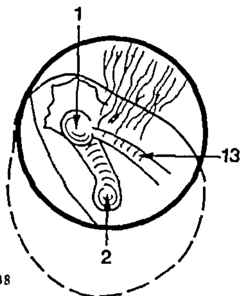
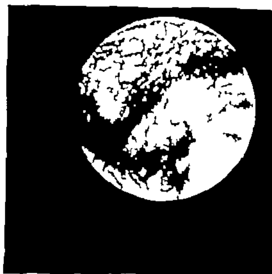
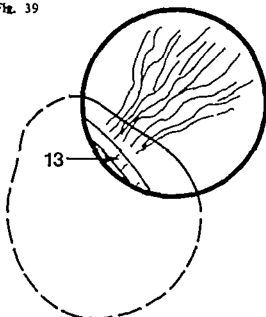
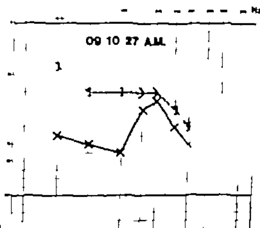


Fig. 38

Fig. 39







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Increased clinical activities with the middle ear Because of the many functional, diagnostic and therapeutic problems from the middle ear one can expect increased clinical activities dealing with the middle ear and the conductive deafness due to causes arising here

The case materials with conductive deafness which need investigation and treatment are also

expected to become more numerous, though antibiotics have made acute middle ear affections less frequent. (Chronic middle ear cases, on the other hand seem to appear with about the same frequency) According to clinical experience there are several reasons, that the following middle ear affections will occur more frequently

a) allergic middle ear manifestations
b) middle ear malformations on toxic or teratogenous grounds
c) traumatic middle ear lesions from traffic accidents
d) middle ear tumors discovered because of increased activity in diagnosis and therapy
e) latent middle ear affections with adhesive and osteitic processes from the use of antibiotics
f) aero-otitis because of the successive increase of air-born transportation Cases with hyperemia, transudation or bleeding may result in adhesive processes

All the above mentioned conditions and clinically manifested tendencies will require an increased use of otomicroscopy together with all available accessories These activities will probably ameliorate the investigation technique by developing new instruments and methods. This may represent, what Kobrak describes as an "M D -otology" besides a purely theoretical *Ph D -otology*"

CLINICAL EXPERIENCES AND INVESTIGATIONS

Some clinical experiences from the oto-audiological team work (consisting of totally 50 E.N T specialists including junior doctors in postgraduate training) are referred to

1 An important part of this work has been to examine and evaluate conductive hearing loss cases It has turned out, that there is a substantial overlapping by two major patient groups those cases to be operated upon and those needing hearing aids It is also found, that with conventional examination technique, using ear speculas without magnification, even experienced otologists may overlook clinically important middle ear details Thus these factors *represent a certain problem of organisation.*

2 A most valuable instrument required in this clinical work is the meticulous *otomicroscopy* It was documented by a detailed analysis of 100 consecutively examined cases, admitted for evaluation of conductive deafness (except otosclerosis) that otomicroscopy revealed to be *the essential part of the investigation as a basis* for diagnosis Different functional tests provided *supplementary information in part of the cases.*

3 Experience has shown, that both for clinical and for didactic reasons, documentation and presentation of essential facts from the investigations of hearing loss patients have to be presented continuously at regular staff meetings.

4 These two basic requirements were the incentives to develop a *routine technique for color photography of otomicroscopical findings* to be used as a standard clinical tool The new commercially available, photoaccessories to Zeiss operation microscope and new types of films with sufficient sensitivity constituted important steps toward getting acceptable pictures. The main problem is still to get sufficient light through the ear speculum on the drum and middle ear which is not as a rule possible with *the ordinary 50 W lamp* This has to be replaced by a device of our own construction, utilizing a halogen lamp of 250 W and also a fan to neutralize the heat production etc. The ear speculas are painted grey in such a way that *light reflection resembles that of the skin,* which permits an automatic production of colored papercopies to be used in the journals

5 The aim of the clinical discussion where the pictures constitute a detail is to *document the otoscopic findings and correlate them with various functional tests*

Emphasized by Kobrak it is very difficult in diseased ears, to assess the different physical factors of sound conduction as to their individual role in causing hearing loss *So far at*

tempts with this aim in mind do not seem to have been fruitful. On the other hand, it seems clinically meaningful to combine the *observation* of changed and damaged middle ear details with an *evaluation* of how pathology may influence the conductive apparatus concerning its clinically comprehensible functions, *i.e*
sound collection
sound conduction
sound protection

With an experience of a substantial case material, discussed and evaluated in this way this technique has been found to be useful in the clinical work and for didactic purposes. This type of documentation makes it possible to demonstrate the essential facts from a large group of patients during few conference hours

The slides with transparent color pictures and the journals with sketches and paper copies in color form such a good basis for clinical decisions that additional visits of the patients to the clinic for further inspection etc are often not necessary

Development of the otomicroscopic approach Otomicroscopical observations of middle ear conditions will probably be still further utilized as a correlate to different diagnostic and therapeutic measures, thus contributing to the amelioration of these methods. During the last decades many steps forward have been made concerning the otomicroscopical technique and also the mode of working

Therefore the next step in this development should be the construction of a suitable otomicroscope which could make the otomicroscopic approach a standard in most clinical work The pictures, presented here, are produced by amateurs and they constitute principally a clinical aid With elaborate, well fitted equipment, it is reasonable to assume that otomicroscopical photos will be a requisite in the journals just like audiograms and other test results. It also seems likely that such an otomicroscopic approach in the clinical work will become an incentive to research of the middle ear with all possible methods.

SUMMARY

In the oto-audiological cooperation there is a substantial overlapping between two major groups of patients, those needing a hearing aid and those needing otosurgery according to the primary examination This fact means a certain problem of organization

The otomicroscopical examination has turned out to be a most useful instrument in this connection. In 100 cases of conductive deafness (except otosclerosis) the otomicroscopic findings revealed to be essential for the diagnosis in the great majority of cases The functional tests, performed, are giving supplementary diagnostic information in part of the cases

Both from clinical and didactic reasons documentation of the otomicroscopic findings is necessary and the clinical discussion requires simultaneous presentation of these findings together with the results from various clinical and functional tests.

This clinical praxis was the incitement to develop a routine technique for color photography of the otomicroscopic findings from the drum and middle ear which could be made by means of some special accessories to a Zeiss operation microscope.

A series of cases with different conductive pathology are presented. The observations of the otomicroscopical findings are correlated with the audiograms and functional tests.

An evaluation is also made of how pathology has changed the clinically comprehensible elements of the conductive mechanism—the sound collection, the sound conduction and the sound protection.

To raise the quality of otoscopy it seems meaningful to construct a suitable otomicroscope with photo equipment to be used in most clinical work The present work has shown, that even with an equipment, partly consisting of accessories, made in the laboratory of the audiological unit, this technique can be clinically utilized.

This also forms a basis for a more functional-

clinical approach at the assessment of cases with conductive deafness

ZUSAMMENFASSUNG

Die Mehrzahl der Fälle mit Mittelohrschwerhörigkeit lässt sich hinsichtlich ihrer Behandlungsmöglichkeiten zwei grossen Gruppen zuordnen Das sind einmal die Fälle für die eine *Operation die gegebene Indikation ist, und zum* andern die Fälle für die ein Hörgerät die gegebene Hilfe ist Zwischen diesen beiden Gruppen findet sich jedoch eine recht grosse Reihe von Fällen bei denen es sehr schwierig ist, von der primären Untersuchung her in dieser Hinsicht eine Entscheidung zu treffen In diesen Fällen hat sich die otomikroskopische Untersuchung als ein für die Diagnose sehr wesentliches Komplement erwiesen

In einer Eingangsstudie von 100 Fällen von *Mittelohrschwerhörigkeit (unter denen sich* wohlgemarkt keine Otosklerosefälle fanden) konnte dies in der grossen Mehrzahl der Fälle durch die otomikroskopischen Befunde klar gezeigt werden Im Zusammenhang damit wurden ausserdem Funktionsprüfungen durchgeführt, aus denen zusätzlich diagnostische Aufschlüsse erhalten werden konnten

Um in der klinischen Diskussion die otomikroskopischen Befunde gleichzeitig mit den Resultaten der klinischen und funktionellen Untersuchungen zugänglich zu haben wurde eine spezielle Aufnahmeapparatur entwickelt, mit der es möglich war Farbphotographien von den otomikroskopischen Befunden vom Trommelfell und Mittelohr zu machen Als Aufnahmeinstrument diente ein Operationsmikroskop der F Zeiss mit eigens konstruierten *Zusatzeinrichtungen u.a um die Beleuchtungsstärke* in dem erforderlichen Masse zu erhöhen.

Ca. 1000 Fälle mit unterschiedlicher Mittelohrpathologie wurden auf diese Weise untersucht Eine Reihe von diesen Fällen werden des näheren gezeigt und ihre otomikroskopischen Befunde mit den Tonaudiogrammen und Funktionsprüfungen korreliert Des weiteren werden die Auswirkungen der pathologischen Veränderungen im Mittelohr auf den Schalleitungsmechanismus und den Schallschutz des Ohres *erörtert*

Aus den vorliegenden Untersuchungen dürfte zur Genüge hervorgehen dass es zur Verbesserung der otomikroskopischen *Untersuchungsmöglichkeiten* sehr zu begrüssen wäre ein entsprechendes Standardmikroskop mit den notwendigen Photomöglichkeiten in der routineklinischen Arbeit zugänglich zu haben

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Light-induced and spontaneous variations in the amplitude of the electro-oculogram

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LIGHT INDUCED AND SPONTANEOUS VARIATIONS IN THE AMPLITUDE OF THE ELECTRO OCULOGRAM

BY

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TURKU 1970

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I Introduction and aim of present investigation

Recording of spontaneous or induced nystagmus with the aid of electro-nystagmography is an essential part of modern neuro-otological examination. In the living human eye an electrical potential difference can be recorded between the anterior and posterior segments of the eye. Thus, with two recording electrodes suitably positioned in contact with the skin near the lateral canthi of the lids of the two eyes movements of the eyes can be recorded as a result of alterations in the electrical field of the surrounding conducting media. On the other hand, the fact that the voluntary eye movements performed are constant in magnitude and direction provides the possibility of recording a constant fraction of the corneo-fundal potential (electro-oculogram, EOG) It has been suggested that in the healthy human eye the corneo-fundal potential may show considerable spontaneous variation. It is also well known that typical changes in the level of the corneo-fundal potential can be produced by changes in retinal illumination. Therefore the amplitude of the electro-nystagmogram (ENG) is influenced not only by the amplitude of the nystagmus to be examined, but also by the level of the corneo-fundal potential difference at the moment of recording.

In the present study the magnitude of spontaneous variation in the corneo-fundal potential (EOG) as well as the effects of constant periods of darkness and illumination on its amplitude have been investigated in order to determine what are, for this purpose, adequately reliable conditions for clinical recording of the electro-nystagmogram

II Earlier investigations

1 Site of origin of the corneo-fundal potential

In the living eye an electrical potential difference can be recorded between the cornea and the posterior pole of the eye. It has been known since the time of Du Bois Reymond (1849) that in vertebrates the cornea is positive in respect to the fundus whereas *in invertebrates* (Dewar and Mc Kendrick 1876) *the potential gradient is reversed* This suggests that this potential difference (standing potential corneo-*fundal potential*) *is* generated in the retina Later this view was confirmed by the finding of an abrupt alteration in the potential at the lateral edge (ora serrata) of the retina (de Haas 1903 as quoted by Kohlrausch 1931) It was also confirmed that an equally large potential difference could be recorded across the isolated retina and across the unopened eye (Kühne and Steiner 1881)

Recently Noell (1953) has shown that drugs which selectively alter the standing potential can be shown to cause extensive damage in the pigment epithelium. It is also evident from the micro-electrode studies of Brindley (1956a) as well as of Brown and Wiesel (1958) that one of the charged membranes in the retina across which a large potential difference is generated can be localized in the pigment epithelium

In the human eye a fraction of the corneo-fundal potential difference can be recorded with electrodes placed on the skin on both sides of the eye and then rotating the eye in the plane of the electrodes through a constant angle It has been shown that the amplitude of this eye movement potential bears a simple relationship to the degree of rotation of the eyes (Fenn and Hursh 1937 Lekselл 1939)

This provides us with a relatively accurate method of measuring eye movements On the other hand the same method can be applied as a clinical test (Arden and Kelsey 1962a) to measurements of the functional state of the pigment epithelium In pathological conditions for example *pigment degeneration of the retina* and detachment of the retina the clinical record *of the corneo-fundal potential shows an abnormally low amplitude and the light induced in*crease in the amplitude of this potential is defective (Arden Barrada and Kelsey 1962) These authors concluded that in order to obtain a normal electro-oculogram the following are required functioning receptors a functioning pigment epithelium contact between the neural structures of the retina and the pigment epithelium as well as adequate choroidal and retinal blood supplies Light that evokes an increase in the amplitude of the corneo-fundal potential generated in the pigment epithelium is probably absorbed in the retinal receptors. This view is supported by the spectral sensitivity measurements of the light induced increase in the corneo-fundal potential performed by Elenius and Leitonen (1962) and Elenius and Karo (1966)

In addition to the corneo-fundal potential generated in the pigment epithelium smaller potential differences can be recorded in the anterior segment of the eye (cornea aqueous ciliary body Lehmann and Meesmann 1924 Potts and Modrell 1957 Stepanik 1958) or between the anterior and posterior poles of the lens (Brindley 1956b)

2 Effects of illumination and darkness on the amplitude of the electro-oculogram of the human eye

It has been known since the work of Kühne

and Steiner (1881) as well as Hiabstedt and Nagel (1902 as quoted by Kohlrausch 1931) that illumination alters the potential difference which in animal eyes can be directly recorded between the cornea and the posterior pole of the eye. In the human eye Miles (1940) made systematic studies on the effects of rapid changes of illumination on the amplitude of the EOG He found that this amplitude was practically constant in constant illumination, whereas reduction in illumination by three logarithmic units decreased the amplitude by 10 per cent within 5 minutes and by 20 per cent within 10 minutes On the other hand an increase in illumination to the previous level (5 mLa) increased the amplitude of the EOG by 43 per cent above the value previously recorded after 10 minutes in the dark. Correspondingly Aserinsky (1955) found that after 10 minutes illumination the amplitude of the EOG was increased by 11 to 208 per cent above the value measured after an equally long period in the dark. Aserinsky (1955) also found that when the eye was stimulated by a succession of alternating periods of illumination and darkness the amplitude recorded after the second period in the dark was significantly smaller than after the first period in the dark. However after several dark (and light) periods a constant level of minimum amplitude was obtained. On the other hand, after long period in the dark (sleeping over night in darkness) the amplitude of the EOG recorded early in the morning was found to be 29 to 51 per cent larger than the amplitude previously measured in the evening at the end of the second short period of dark-adaptation. In agreement with Miles (1940) and Aserinsky (1955) Ten Doesschate and Ten Doesschate (1956) found that the amplitude of the EOG decreased during dark-adaptation and increased during light-adaptation while the results of Francois, Verriest and De Rouck (1955) suggest that in this respect the effects of light and darkness on the EOG are totally reversed. Using longer periods of dark-adaptation than previous authors Ten Doesschate and Ten Doesschate (1956) were also able to detect a secondary slow increase in the amplitude of the EOG after the minimum found on the average after 10 minutes in the dark. This is in agreement with the theory put forward by Kris (1958) and Kolder (1959) that the effects of light on the EOG resemble a process of damped oscillation of this potential In the human eye the peak and trough times of these oscillations occur within the following ranges first peak at 10 min ± 2 min, first trough at 25 min $\pm$ 4 min and second peak at 36 min $\pm$ 4 min (Kris, 1958) The amplitude of the first peak varies with the logarithm of retinal illumination and with the duration of preliminary dark adaptation (Arden and Kelsey 1962b) Only the size of the first peak depends on the intensity of illumination, while the amplitude of the second and third peaks and the amplitude of the trough do not vary with the intensity of illumination (Kolder, 1959) A logarithmic relationship between the energy of the light stimulus and the light-induced increase in the amplitude of the rabbit's EOG was reported by Heck and Papst (1957)

Recently Kolder and Brecher (1966) have contributed to the understanding of the oscillating nature of the alterations in the amplitude of the human EOG induced by light and darkness by describing in addition to the slow oscillatory process another type of oscillation of much higher frequency They showed that the slow oscillatory process of the indirectly recorded human corneo-fundal potential can be brought into synchrony when the eye is stimulated with repeated light and dark phases of equal duration (12.5 minutes) In addition to this slow oscillatory process (one period lasting 25 to 30 minutes) a transient fluctuation of the corneo-fundal potential follows immediately upon a change from light to dark or from dark to light. This initial transient fluctuation has been previously described (Aserinsky 1955 Kris, 1958 Kolder 1959 Arden and Kelsey 1962a) Kolder and Brecher (1966)

showed that a fast oscillatory process of the corneo-fundal potential can be evoked by stimulation with repeated short periods of light and darkness and can be brought into synchrony with light and dark periods of equal duration (1 1 minutes) As compared with the slow oscillatory process the fast oscillations are opposite in direction the change in the amplitude being reduced by illumination and increased by darkness

3 Spontaneous variation in the amplitude of the electro-oculogram of the human eye

There are several reports showing the large individual variation in the amplitude of the EOG (MOWRER RUCH and MILLER 1936 FENN and HURSH 1937 MILES 1939 MACKENSEN and HARDER 1954 FRANCOIS VERRIEST and DE ROUCK 1956 KOLDER 1959 SHACKEL 1960 ARDEN and BARRADA 1962 ELENIUS and KARO 1966) In 52 healthy subjects examined by ARDEN and BARRADA (1962) the range of variation in the amplitude of the light peak potential was reported to be 15 3 to 66 7 μV/degree of eye rotation (high illumination 3000 troland) and 14 0 to 80 0 μV/° (low illumination 350 troland) respectively Correspondingly in ten subjects examined by ELENIUS and KARO (1966) the average light peak amplitude (obtained after 8 minutes of illumination with blue light of 330 000 photopic troland intensity) was found to be 1 5 mV/45 degrees of eye rotation (33 3 μV/°) the extreme individual values being 0 85 and 2.25 mV/45° (18.8 and 50 μV/°) A review of the results of earlier work in this field based on measurements made with widely differing recording techniques (recalculated in μV) was published by ARDEN and BARRADA (1962)

FENN and HURSH (1937) and MILES (1939) as well as MACKENSEN and HARDER (1954) found variations of the order of 50 per cent (increase or decrease) in the amplitude of the EOG measured in the same subject on two consecutive days ASERINSKY (1955) observed that a regular increase in the amplitude of the EOG occurred during the night the amplitude measured in the morning being 29 to 51 per cent larger than the amplitude measured the previous evening This is not in agreement with a report by KRIS (1960) of a regular diurnal variation in the amplitude of the EOG amplitudes being lowest early in the morning and greatly increased (doubled or even trebled) by noon

DAVIS and SHACKEL (1960) were unable to confirm the results of KRIS (1960) In fact they found that in one subject the amplitude of the EOG changed in the course of the day by as much as 300 μV although in most cases it remained almost unaltered The variation in the amplitude that occurred within a week was also found to be relatively limited. This variation was on the average 46 μV and less than 105 μV in 95 per cent of cases whereas the variation in the amplitude observed within 24 hours was somewhat larger (on the average 76 μV) A slight reduction in the amplitude of the EOG in the course of the day has been reported by AANTAA and ELENIUS (1968) Their measurements were made at 8 a.m and 8 p.m using light induced amplification of the EOG after 8 minutes of illumination with light of 10 000 troland intensity following a period of dark adaptation of 15 minutes duration In their results the reduction in the amplitude that occurred between 8 a.m and 8 p m was on the average 10 per cent Stimulation with light was also used by KELSEY (1967) who investigated the variation in the relationship between the light peak and the dark trough of the EOG measured at intervals of one week No correlation was found in the female subjects of this study between the variation in the ratio (light peak / dark trough × 100) of the EOG and the menstruation or ovulation cycle

III Methods material and procedure

In most experiments the electro-oculogram was recorded with a condenser-coupled differential amplifier connected to a pen recorder (Electronystagmograph, Madsen Electronics) The amplification used was 1250 μV/cm and the time constant 2 seconds Conventional lead electrodes (7 mm in diameter) were used. The electrodes were attached to the skin with adhesive tape, and electrode jelly was used to improve the contact. The ground electrode was attached to the skin of the forehead In one series of experiments the D.C. differential amplifier of a Tektronix 502 oscilloscope and chlorinated silver electrodes (6 mm in diameter) were used. Calibration of the amplified signal (horizontal eye movement of constant magnitude) was performed by using both amplifier systems simultaneously so that the deflection of the pen recorded on the electro-nystagmograph could be related to the signal amplified by the D.C. amplifier and observed on the oscilloscope screen as well as to the internal calibration of the Tektronix oscilloscope. Most experiments were performed in the routine ENG laboratory In this room the walls are white and the ceiling matt grey however even in the day time the room could be made almost dark by drawing curtains over the windows Two small lamp bulbs were used as fixation lights The intensity of the fixation lights could be adjusted so that they were visible but not too bright both during illumination and in the dark. The test subjects were trained to make rapid horizontal eye movements on command from one fixation light to the other and they were instructed not to make compensatory head movements In the experiments made in this laboratory the subjects were in recumbent position with the head slightly elevated on a cushion. Thus the subject was in a comfortable position to look at the fixation lights located on the upper part of the opposite wall. In those experiments in which stimulation with light was used, the white light was produced with a Leitz projector and projected to form a square (80 × 80 cm) image on the wall between the two fixation lights. One series of experiments (measurements of the velocity of eye movements) was performed in the dark room of the department of ophthalmology The walls and ceiling of this room are black and there is no window In these experiments the subjects were in a sitting position and the fixation lights were located on the opposite wall at the level of the subject s eyes.

The subject tested were both men and women aged 20 to 25 Most of them came from the local Medical School or the Nursery School. Total material consists of 210 subjects (155 women, 55 men) They had all been found on examination to have healthy eyes Cases with low visual acuity or with errors of refraction exceeding + 2 or —2 d were excluded and so were cases with apparent heterophoria or squint. The subjects lived fairly regular lives and were not involved in night work during the period of the tests For dilatation of the pupils Mydriat eye drops (Orion) were used.

In different series of experiments of the present study there were variations in the amplifiers and electrodes used, in the magnitude of the horizontal eye movement (angle between fixation lights) in the sequence and duration of the dark and light periods employed as well as in the intensity of illumination. Therefore, to facilitate reading some details of the methods and procedure are given or repeated in the beginning of the respective sections on the results.

Diurnal variation in the resistance of the skin was examined by placing one of the lead

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Diurnal variation in the resistance of the skin was examined by placing one of the lead

electrodes used in the present study on the skin near the temporal canthus of the lids of the left eye The skin was cleaned by rubbing with cotton soaked in 50 per cent ethyl alcohol and electrode jelly was used to improve contact *with the skin this procedure as well as the* location of the electrode thus being identical with that used in most of the other experiments of the present study The electrode-skin resistance of this single electrode was then measured with a Mingograph (Elema-Schönander) electroencephalograph using o group of twenty EEG electrodes (as in EEG recording) in combination as the other measuring electrode These electrodes were located on the skin of the skull the skin under each electrode having been drilled so that the combined resistance of the group of electrodes was minimal A 12-cycle alternating current signal was used for the measurements the amplitude of the recorded sinusoidal oscillation being proportional to the skin-electrode resistance of a single electrode (10 mm corresponding to 10 kilo-ohms) A group of 148 subjects (average age 44) was examined before 10 a.m and another group of 148 subjects (average age 42) was examined after 2 p m *It was found that the average resistance obtained* in the morning was 1.57 kilo-ohms as compared with 1.55 kilo-ohms in the afternoon

In the present study photometry was carried out with a calibrated luxmeter (Svenska Ljuskultur Stockholm) The luminance (apostilb) of the opposite wall was calculated from the measurements obtained in lux units by multiplying by an approximate reflexion factor of 0 8 (10 apostilb = 1 millilambert) Retinal illumination (troland) is obtained by multiplying the luminance converted to nit units (1 apostilb = 0 318 nit) by the pupil area (mm^2)

The statistical significances were tested by Student s t test

IV Results

1 Amplitude of the electro-oculogram as affected by the position of the recording electrodes

MACKENSEN and HARDER (1954) have shown that the amplitude of the EOG decreases as the distance between the electrodes increases It is also evident (MOWRER, RUCH and MILLER, 1936 KRIS, 1960) that maximal amplitude of the EOG is obtained by moving the eyes in the plane corresponding to that of the pair of electrodes.

Table 1 Amplitude of the EOG with different locations of the recording electrodes

Location of the electrodes	Mean amplitude of the EOG (1 mm corresponds to 125 μV) and standard deviation as measured in 15 subjects and expressed in mm of the amplitude recorded by making 30-degree horizontal excursions of the eyes.	Average amplitude of the EOG as percentage of the amplitude recorded with electrodes in the primary position
Near the canthi of the lids of both eyes	Mean 7.21 S.D 1.27	100
One electrode displaced 1 cm laterally	Mean 7.23 S.D 1.40	93.8
Both electrodes displaced 1 cm laterally	Mean 6.42 S.D 1.29	83.3
Lateral displacement of one electrode by 1 cm and the other by 2 cm	Mean 5.53 S.D 1.10	71.9
Both electrodes displaced 2 cm laterally	Mean 4.63 S.D 0.85	60.2

For the purposes of the present study the influence of the location of the electrodes on the amplitude of the EOG was investigated in the eyes of 15 (10 men and 5 women) subjects aged 20 to 25

Lead electrodes 7 mm in diameter were used. In the original (primary) position the two recording electrodes were placed on the skin near the temporal canthi of the lids of the two eyes (the earthed electrode was placed on the skin of the forehead) In the subjects tested, the distance from the canthus of the lids to the nearest edge of the electrode varied from 14 to 16 mm. In the course of the experiment the position of the recording electrodes was altered by making 1 cm lateral displacements of one or both electrodes. Several recordings of the EOG were made using different electrode positions. The subject was in a recumbent position and, on command, made horizontal 30-degree excursions of the eyes. Two small fixation lights were used to control the magnitude of the movement, as well as to restrict the direction of movement of the eyes to the plane of the electrodes. A condenser-coupled differential amplifier connected to a pen recorder (amplification 1250 μV/cm, time constant 2 sec) was used Before beginning the experiment the subject was dark-adapted for 30 min.

The results are shown in Table 1 and Fig. 1 It is evident that the amplitude of the EOG decreases as the distance between the electrodes increases An increase of 1 cm in the inter electrode distance (one electrode displaced 1 cm laterally) corresponds to an average decrease in the amplitude of the EOG to 93 per cent of the original level. Analogously a 2 3 or 4 cm increase in the distance between the electrodes produces an average decrease in the amplitude of the EOG to

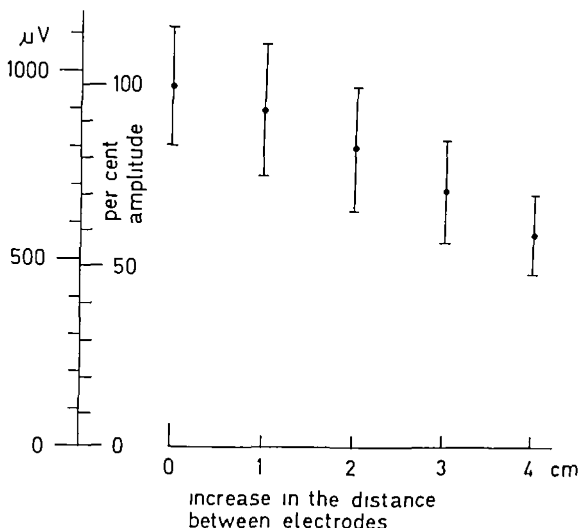


Fig. 1. Average amplitude of the EOG (dots, 15 subjects) in µV and as a percentage of the amplitude measured with recording electrodes in the original (primary) position as plotted against laterally increased distance between the electrodes. Vertical bars indicate 2 × standard deviation.

83, 72 and 60 per cent of the original level. An increase in the inter-electrode distance of 2 or 4 cm was obtained by symmetrical lateral displacement of both electrodes, whereas in order to produce an increase of 1 or 3 cm in the distance one electrode was displaced 1 cm further laterally than the other.

It is interesting to note that, for example, a decrease in the amplitude of the EOG by an average of 10 per cent below the original level corresponds to an increase in the inter-electrode distance of more than 10 mm. It is most unlikely that an unobserved displacement of the electrodes of this order of magnitude could occur in a series of controlled experiments. In all the subsequent experiments of the present study in which the same subject was examined on several occasions the location of the electrodes was marked with ink on the skin. Therefore the correct position of the electrodes could be ensured within the limits of 1 mm displacement of each electrode.

2. Electro-oculographic measurements of the velocity of horizontal voluntary eye movement

Measurements of the maximal velocity of a horizontal gaze movement were performed on 10 subjects (5 women and 5 men) aged 20 to 25. Each subject was examined twice on the same day, namely at 8 a.m. and 8 p.m.

Chlorinated silver electrodes and maximal amplification (200 µV/cm) of a D.C. differential amplifier of a Tektronix 502 oscilloscope were used. The velocity of the sweep was 50 msec/cm. Markings made with ink on the skin made it possible to place the recording electrodes in the same position in the morning and in the evening. The subject was seated in a chair It was checked that compensatory head movements could not be made. A cushion placed behind the head and neck helped to hold the head steady There were two small fixation lights placed on the opposite wall at the level of the subject's eyes. The distance between the two fixation lights in relation to the distance of the eyes from the wall (260 cm) made an angle of 40 degrees. The subject was instructed to look at the left fixation light and on command to move the eyes straight from the left to the right fixation light. Simultaneously with the command to the right a beam of light was flashed on the right fixation light and a restricted (15 cm diameter) area surrounding it. Part of the same beam was reflected on a barrier layer photocell to produce a triggering pulse for the sweep of the C.R.O Synchronization of the start of the sweep with the start of the gaze movement greatly facilitated the recordings. On the other hand, the fact that a light signal was flashed on the right fixation light simultaneously with the verbal command to the right aided orientation of the gaze movement.

The recordings were either made directly (visually) from the trace afterglow on the oscilloscope screen or were photographed One

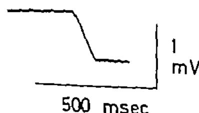


Fig. 2. An EOG (photographed from the oscilloscope screen) recorded with the aid of D.C. differential amplifier. The change in the potential level refers to horizontal gaze movement from left to right through an angle of 40 degrees.

Table 2. Average time (10 measurements) taken to make horizontal gaze movement (from left to right) through an angle of 40 degrees as measured in 10 subjects at 8 a.m. and 8 p.m.

	8 m. msec	8 p.m. msec
	92.5	90.0
	71.0	72.5
	90.0	89.5
	94.5	94.0
	90.5	90.5
	95.0	98.5
	89.0	90.0
	100.0	100.0
	74.0	74.5
	73.5	74.5
Mean	87.0	87.0
S.D	10.5	10.0

original recording is illustrated in Fig. 2. All recordings were performed 20 minutes after the beginning of the experiment. The subject spent this preliminary period in a dimly illuminated examination room (2 lux illumination as measured in front of the eyes pupils not dilated) with his eyes closed to acquire a constant state of visual adaptation. Then several recordings were made in rapid succession to obtain a series of at least ten reliable measurements for every case.

The results (averages of ten measurements) are given in Table 2 and show that in the ten cases tested there was no observable difference between measurements made in the morning and in the evening, whereas in individual cases, both in the morning and in the evening, there was a large variation in maximal velocity of the horizontal gaze movement, the extreme values being 71 msec/40 degrees and 100 msec/40 degrees respectively

3 Light-induced changes in the amplitude of the electro-oculogram

In the first part of the present series of experiments the general effects of light and dark-adaptation on the amplitude of the EOG were examined. It was considered important to know about the effects of the standard illumination of the routine electro-nystagmography laboratory

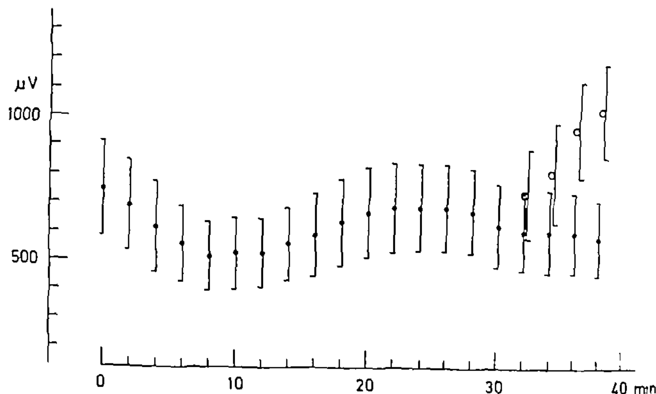


Fig. 3. Amplitude of the EOG as measured in the dark (dots) and during illumination (circles). Averages of measurements made on 20 subjects (dots, 0 to 30 min), 10 subjects (dots, 32 to 38 min) and 10 subjects (circles, 32 to 38 min). Vertical brackets show 2 × standard deviation.

room on the amplitude of the EOG recorded after a period in darkness. The experiments were made at different times of day and the subjects came to the examination room from widely differing illumination conditions. A long preliminary period of dark-adaptation was therefore considered necessary. After this period (30 min) the standard illumination of the examination room was turned on and the increase in the amplitude of the EOG was tested in ten subjects, whereas in another series of ten subjects, employed as controls, the dark-adaptation was continued. The standard illumination of the examination room consists of two series of three (60 cm, 20 W) fluorescent tubes mounted uncovered in the ceiling. The matt grey ceiling has a relatively low capacity as a light diffuser, whereas the walls of the room are white. The curtains were drawn over the windows. During the experiments the subjects to be examined were in a recumbent position facing two small fixation lights on the opposite wall (30 degree angle between the fixation lights). During the period in the dark the subject was asked to keep his eyes closed. Conventional lead electrodes and a condenser-coupled differential amplifier connected to a pen were used for the recordings, the experimental conditions thus being identical to those used in this laboratory for routine ENG recordings.

Twenty women aged 20 to 25 were examined. The pupils were not dilated. The intensity of illumination used in these experiments was 130 lux as measured in front of the eyes with the photocell of a luxmeter placed perpendicularly to the direction of the eyes when looking at the fixation lights. The maximal luminance of the upper part of the opposite wall (above the fixation lights) was estimated to be 25 mLa, corresponding to 1000 troland (4 mm average diameter of the pupil during illumination). The luminance of the opposite wall was not uniform and it should also be noted that the six fluorescent tubes placed in the ceiling were

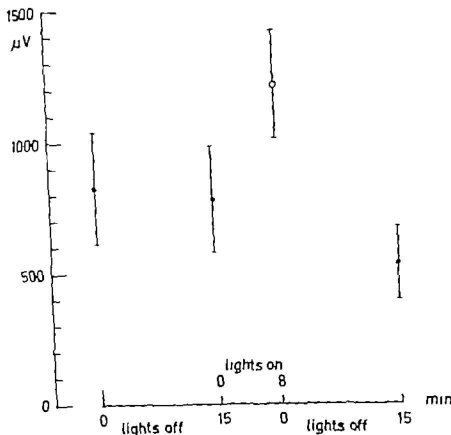


Fig. 4. Amplitude of the EOG measured at the beginning of the experiment and after the following periods. 15 minutes in the dark, 8 minutes of illumination with light of 10 000 troland intensity and 15 minutes in the dark. The dots and the circle show averages of measurements made on 56 subjects. vertical bars show 2 × standard deviation

within the upper part of the visual field when the subject looked at the level of the fixation lights.

The EOG was recorded every two minutes both in the dark and during illumination. The individual measurements given are average amplitudes of a series of at least ten electro-oculograms recorded. The results are shown in Fig. 3. It is evident from the averages of the results obtained in the ten subjects shown in this illustration (dots, vertical brackets show 2 × standard deviation) that a steady amplitude of the EOG is not achieved. In the dark there is first a reduction in the amplitude of the EOG followed after 10 to 12 minutes by a secondary increase which approaches its maximum after 24 to 26 minutes in the dark. Then the amplitude again shows a slow decrease. In the ten subjects tested during illumination as well (circles, vertical brackets show 2 × standard deviation) there is a definite increase in the amplitude above the level measured in the ten controls continuously tested in the dark.

The average minimum amplitude obtained after 8 minutes in the dark is 32 per cent below the level of the amplitude measured at the beginning of the experiment. The average maximum amplitude obtained 8 minutes after stimulation with light (38 minutes after the beginning of the experiment) is 39 per cent above the level measured at the beginning of the experiment. It is thus evident that considerable

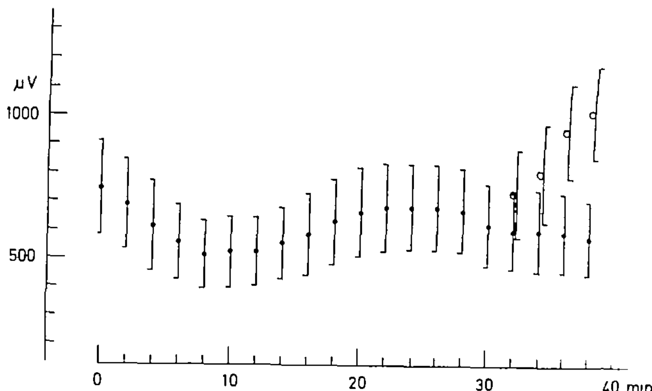


Fig 3 Amplitude of the EOG as measured in the dark (dots) and during illumination (circles) Averages of measurements made on 20 subjects (dots, 0 to 30 min) 10 subjects (dots, 32 to 38 min) and 10 subjects (circles 32 to 38 min) Vertical brackets show 2 × standard deviation.

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Table 4. Mean amplitude (mm, 1 mm refers to 125 µV), standard deviation and coefficient of variation of the EOG. The results refer to measurements performed on 92 subjects at the beginning of the experiment and after 8 minutes' illumination with light of 10 000 troland intensity (following a 15-minute period of dark-adaptation). Measurements made in the morning (8 a.m.) and in the evening (8 p.m.) have been combined.

	Mean amplitude	Standard deviation	Coefficient of variation
In the beginning of the experiment	5.31	1.65	0.309
After 8 minutes' illumination	8.17	2.06	0.206

the amplitude of the EOG but also decreases the variation in the measurements of the amplitude.

This is further supported by results obtained in two additional series of experiments. In 22 subjects, each of them examined four times during the same day (8 a.m., 12 a.m., 4 p.m. and 8 p.m.) there was only moderate diurnal variation in the coefficient of variation, whereas at each of the times of day examined the coefficient of variation was smaller after 8 minutes' stimulation with light than at the beginning of the experiment or after dark-adaptation (Table 3). The differences are statistically significant, $p < 0.01$.

The coefficient of variation was also calculated for a greater number of subjects (92 subjects) examined both at 8 a.m. and 8 p.m., the results obtained in the morning and in the evening (as well as some of the results obtained in the 22 subjects described above) being now included in the same experimental group (184 observations). It is evident from these results (Table 4) that in the beginning of the experiment, when the average amplitude of the EOG is 5.31 mm (660 µV), the coefficient of variation is 0.309, whereas after 8 minutes' illumination with light of 10 000 troland intensity the amplitude is increased to an average of 8.17 mm (1025 µV) and the coefficient of variation is reduced to 0.252. The difference is statistically significant, $p < 0.01$.

4 Spontaneous variations in the amplitude of the electro-oculogram

It has been shown above that the amplitude of the EOG can be greatly increased, and the variation in the amplitude in constant conditions can be reduced by stimulation with light following dark-adaptation. Therefore, in the present study light-induced amplification of the response has been applied systematically to a large series of experiments concerned with spontaneous variations in the amplitude of the EOG. The results of these experiments are presented below.

The light used for stimulation was produced with a "Leitz" projector. Conventional lead electrodes and a condenser-coupled differential amplifier connected to a pen recorder were used, the experimental procedure being identical to

Table 5. Results of diurnal measurements (22 cases) of amplitude of the EOG (mm, 1 mm refers to 125 µV). Four measurements were made in each case at four-hour intervals (as indicated). Each individual measurement is the mean of a series of at least ten responses recorded. The means and standard deviations of the results obtained with 22 subjects are also shown. All measurements were made after an 8-minute period of illumination with light of 10 000 troland intensity following a 15-minute period of dark-adaptation.

	8 a.m.	12 m.	4 p.m.	8 p.m.
	11.2	9.7	9.1	8.2
	11.7	12.6	11.6	9.7
	8.7	7.7	6.7	6.3
	8.2	7.0	6.8	6.3
	10.1	10.7	6.8	9.5
	9.2	10.3	9.2	8.0
	10.3	10.0	10.3	9.5
	8.0	7.9	8.1	6.9
	7.4	8.6	10.0	7.3
	9.4	10.1	9.3	9.8
	11.5	9.4	10.3	10.8
	11.7	10.9	10.1	9.3
	11.2	9.0	9.0	9.6
	11.8	11.1	11.1	9.9
	9.5	11.1	10.1	9.5
	7.1	7.9	7.7	7.7
	11.4	12.0	10.4	8.7
	10.8	8.8	8.5	10.2
	10.1	8.0	9.8	9.0
	10.5	9.0	9.1	7.9
	10.0	9.0	9.0	8.0
	10.0	9.0	10.5	8.8
Mean	10.0	9.3	9.2	8.7
S.D.	1.45	1.48	1.57	1.25

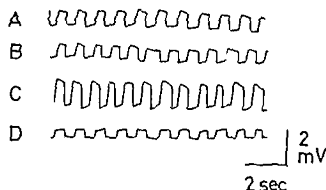


Fig 5 Recordings of the EOG made with a condenser coupled differential amplifier connected to a pen recorder A, at the beginning of the experiment B after 15 minutes in the dark, C, after subsequent illumination with light of 10 000 troland intensity for 8 minutes, D after another 15-minute period of dark adaptation

variation in the amplitude of the EOG occurred in the dark and during illumination with the standard lights of the routine ENG laboratory

In the second part of this series of experiments a special light source a 'Leitz' projector was used for stimulating the eyes with light This light was projected on a white screen placed on the wall between the two fixation lights at a distance of 200 cm from the eyes of the subject On this screen uniform illumination was produced over an area of 6400 cm² (80 × 80 cm square) The pupils were dilated the average pupil diameter during illumination being 7 mm The intensity of illumination on the screen was 80 mLa which corresponds to 10 000 photopic troland. The experimental procedure was the same as described above but all experiments were now performed at 8 a.m and measurements of the amplitude of the EOG were made only at the beginning of the experiment and after the following periods of time 15 minutes in the dark 8 minutes after the beginning of illumination and after a second period of dark-adaptation of 15 minutes duration

The average results obtained in experiments performed on 36 subjects (women aged 20 to 25) are presented in Fig 4 and original recordings of the EOG obtained in one case are shown in Fig 5 It is evident from Fig 4 that stimulation with light increased the amplitude of the EOG on average by 45 per cent above the level measured at the beginning of the experiment This illustration also shows that after a second 15-minute period of dark-adaptation the average amplitude is 32 per cent below the level measured after the first period of dark-adaptation

It was of interest to know whether the variation in the measurements of the amplitude of the EOG could be reduced by increasing the amplitude by stimulation with light. Theoretically the damped oscillatory process of alteration in the amplitude should be "in phase" after stimulation with light following a constant period of dark-adaptation. Calculations based on the results already presented in Fig 4 confirmed that this was the case The coefficient of variation (SD/mean) calculated from results obtained 8 minutes after stimulation with light was 0 165 as compared with 0.266 0.251 and 0.270 for the results obtained in the beginning of the experiment and after the first and second 15-minute periods of dark-adaptation respectively This difference is statistically significant $p < 0.01$ Thus the low coefficient of variation 0 165 obtained after 8 minutes illumination with light of 10 000 troland intensity shows that stimulation with light not only increases

Table 3 Coefficient of variation of the amplitude of the EOG as calculated from results obtained with 12 healthy subjects at the beginning of the experiment and after the following successive periods 15 minutes of dark-adaptation, 8 minutes of illumination with light of 10 000 troland intensity and 15 minutes of dark adaptation. The results refer to experiments performed four times (as indicated) in the course of the same day

	8 a.m.	12 a.m.	4 p.m.	8 p.m.
At the beginning of the experiment	0.223	0 193	0 186	0 165
After 15 minutes dark-adaptation	0 183	0.235	0 230	0 194
After 8 minutes illumination with *light of 10 000* troland intensity	0 145	0 159	0 148	0 143
After second 15-minute period of dark-adaptation	0.228	*0.232*	*0.233*	*0.20.*

Table 4. Mean amplitude (mm, 1 mm refers to 125 μV), standard deviation and coefficient of variation of the EOG. The results refer to measurements performed on 92 subjects at the beginning of the experiment and after 8 minutes' illumination with light of 10 000 troland intensity (following 15-minute period of dark-adaptation). Measurements made in the morning (8 a.m.) and in the evening (8 p.m.) have been combined.

	Mean amplitude	Standard deviation	Coefficient of variation
In the beginning of the experiment	5.31	1.65	0.309
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the amplitude of the EOG but also decreases the variation in the measurements of the amplitude.

This is further supported by results obtained in two additional series of experiments. In 22 subjects each of them examined four times during the same day (8 a.m. 12 a.m. 4 p.m. and 8 p.m.) there was only moderate diurnal variation in the coefficient of variation, whereas at each of the times of day examined the coefficient of variation was smaller after 8 minutes stimulation with light than at the beginning of the experiment or after dark-adaptation (Table 5). The differences are statistically significant, $p < 0.01$.

The coefficient of variation was also calculated for a greater number of subjects (92 subjects) examined both at 8 a.m. and 8 p.m. the results obtained in the morning and in the evening (as well as some of the results obtained in the 22 subjects described above) being now included in the same experimental group (184 observations). It is evident from these results (Table 4) that in the beginning of the experiment, when the average amplitude of the EOG is 5.31 mm (660 μV) the coefficient of variation is 0.309 whereas after 8 minutes illumination with light of 10 000 troland intensity the amplitude is increased to an average of 8.17 mm (1025 μV) and the coefficient of variation is reduced to 0.252. The difference is statistically significant, $p < 0.01$.

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The light used for stimulation was produced with a "Leitz" projector. Conventional lead electrodes and a condenser-coupled differential amplifier connected to a pen recorder were used, the experimental procedure being identical to

Table 5. Results of diurnal measurements (22 cases) of amplitude of the EOG (mm, 1 mm refers to 125 μV). Four measurements were made in each case at four-hour intervals (as indicated). Each individual measurement is the mean of a series of at least ten responses recorded. The means and standard deviations of the results obtained with 22 subjects are also shown. All measurements were made after an 8-minute period of illumination with light of 10 000 troland intensity following 15-minute period of dark-adaptation.

	8 a.m.	12 m.	4 p.m.	8 p.m.
	11.2	9.7	9.1	8.2
	11.7	12.6	11.6	9.7
	8.7	7.7	6.7	6.3
	8.2	7.0	6.8	6.3
	10.1	10.7	6.8	9.5
	9.2	10.3	9.2	8.0
	10.3	10.0	10.3	9.5
	8.0	7.9	8.1	6.9
	7.4	8.6	10.0	7.3
	9.4	10.1	9.3	9.8
	11.3	9.4	10.3	10.8
	11.7	10.9	10.1	9.3
	11.2	9.0	9.0	9.6
	11.8	11.1	11.1	9.9
	9.5	11.1	10.1	9.5
	7.1	7.9	7.7	7.7
	11.4	12.0	10.4	8.7
	10.8	8.8	8.5	10.2
	10.1	8.0	9.8	9.0
	10.5	9.0	9.1	7.9
	10.0	9.0	9.0	8.0
	10.0	9.0	10.5	8.8
Mean	10.0	9.3	9.2	8.7
S.D.	1.45	1.48	1.37	1.25

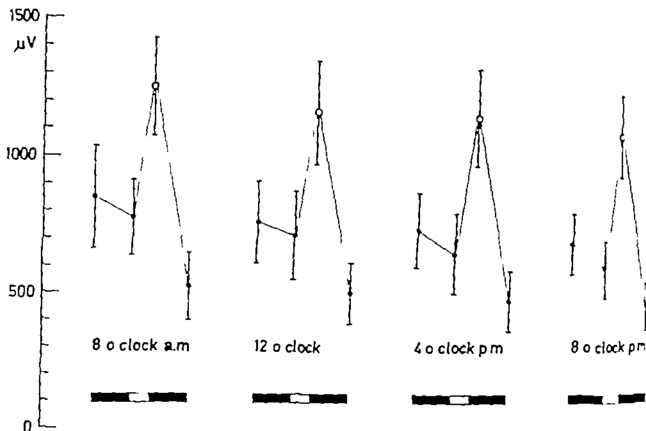


Fig 6 Average amplitude (µV) of the EOG as measured in 22 subjects four times at four-hour intervals as indicated Measurements were made at the beginning of the experiment (dots) and after the following periods 15 minutes of preliminary dark-adaptation (dots), 8 minutes of illumination with light of 10 000 troland intensity (circles) and after a further 15-minute period of dark-adaptation (dots) Periods of darkness and illumination are marked on the abscissa with black and white respectively Vertical bars indicate 2 × standard deviation.

that used in this laboratory for routine ENG recordings However in a part of the study on *diurnal variation in the amplitude* a DC differential amplifier and chlorinated silver electrodes were used The light projected on to a white screen (80 × 80 cm square) placed 2 metres in front of the subject who was asked to look rhythmically between the two fixation lights the eyes thus making horizontal excursions of 30 degrees The measurements made in individual cases refer to the average amplitude obtained in a series of at least ten recordings of the EOG

The diurnal variation in the amplitude of the EOG was investigated in 22 women aged 20 to 25 Each subject was examined four times (at 4-hour intervals) during one day the hours of examination being 8 a m 12 a.m 4 p.m and 8 p m Table 5 shows the average results obtained after 8 minutes stimulation with light (10 000 troland average diameter of the pupil 7 mm) *It is evident that the average amplitude* of the EOG decreases slightly in the course of the day However only the difference between the amplitude measured at 8 a m and 8 p m. is statistically significant ($p < 0\ 001$) the average reduction in amplitude in this case being 13 per cent below the level measured in the morning A statistically significant difference between the measurements made in the morning and in the evening was also found when measurements made after the first period in the dark ($p < 0\ 001$) or after the second period in the dark ($p < 0\ 01$) were used It is also evident from Table 5 that it was only in twelve of the total of 22 subjects tested that the largest amplitude was found in the measurements made in the morning (8 a m) In seven cases the largest

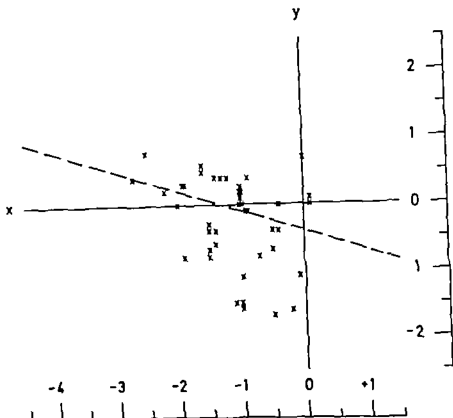


Fig 7 Diagram illustrating measurements made on 92 subjects of the diurnal change (increase +; decrease —) in the EOG potential level obtained after 15 minutes in the dark (ordinate: first dark trough) as related to the corresponding change in the light-induced fraction of this potential (abscissa: from the first dark trough to the light peak illumination for 8 minutes with light of 10 000 troland intensity) The results refer to measurements made at 8 a.m. and 8 p.m. The regression line calculated (y=—0.426—0.293) indicates negative correlation (correlation coefficient —0.329)

amplitude was found at noon in three subjects in the afternoon (4 p.m.) but in no case in the evening (8 p.m.)

The means (μV) and standard deviations of these results are presented in Fig. 6 The results obtained in the beginning of the experiment as well as after a period in the dark after stimulation with light and after a second period of dark-adaptation are shown. It is evident from this illustration that not only the average maximum amplitude (circles) obtained after 8 minutes of stimulation with light but also the decreased amplitude after both the first and the second 15-minute period of dark-adaptation (dots) as well as the amplitude obtained in the beginning of the experiment (dots) all show a slight continuous decrease during the course of the day The ratio of the maximum amplitude (after illumination, circles) to the minimum amplitude (after subsequent dark-adaptation) multiplied by a hundred $\left(\frac{\text{light peak}}{\text{dark trough}} \times 100\right)$ remains fairly constant the values calculated from results obtained at 8 a.m. 12 a.m., 4 p.m. and 8 p.m being *238* *232*, *242* and 242 respectively The corresponding ratios calculated on the basis of measurements made after the first 15-minute period in the dark (before illumination) are 161 163 177 and 181 These ratios show a continuous increase in the course of the day the ratio obtained at 8 p.m. being 12.4 per cent larger than the ratio obtained at 8 a.m.

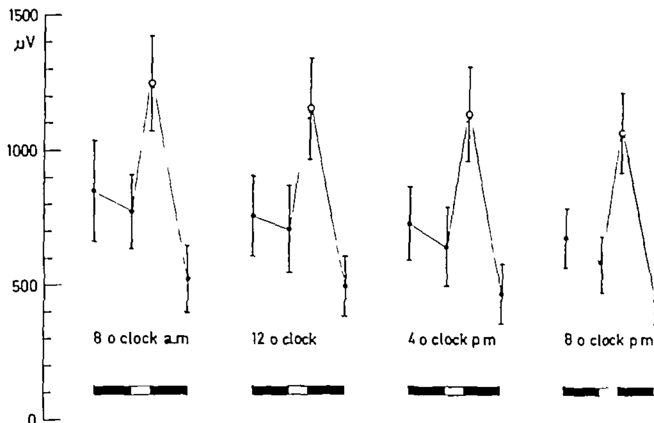


Fig. 6. Average amplitude (µV) of the EOG as measured in 22 subjects four times at four-hour intervals as indicated. Measurements were made at the beginning of the experiment (dots) and after the following periods: 15 minutes of preliminary dark-adaptation (dots), 8 minutes of illumination with light of 10 000 troland intensity (circles) and after a further 15-minute period of dark-adaptation (dots). Periods of darkness and illumination are marked on the abscissa with black and white respectively. Vertical bars indicate 2 × standard deviation.

that used in this laboratory for routine ENG recordings. However, in a part of the study on diurnal variation in the amplitude, a D.C. differential amplifier and chlorinated silver electrodes were used. The light projected on to a white screen (80 × 80 cm square) placed 2 metres in front of the subject, who was asked to look rhythmically between the two fixation lights, the eyes thus making horizontal excursions of 30 degrees. The measurements made in individual cases refer to the average amplitude obtained in a series of at least ten recordings of the EOG.

The diurnal variation in the amplitude of the EOG was investigated in 22 women aged 20 to 25. Each subject was examined four times (at 4-hour intervals) during one day, the hours of examination being 8 a.m., 12 a.m., 4 p.m. and 8 p.m. Table 5 shows the average results obtained after 8 minutes' stimulation with light (10 000 troland, average diameter of the pupil 7 mm). It is evident that the average amplitude of the EOG decreases slightly in the course of the day. However, only the difference between the amplitude measured at 8 a.m. and 8 p.m. is statistically significant ($p < 0.001$), the average reduction in amplitude in this case being 13 per cent below the level measured in the morning. A statistically significant difference between the measurements made in the morning and in the evening was also found when measurements made after the first period in the dark ($p < 0.001$) or after the second period in the dark ($p < 0.01$) were used. It is also evident from Table 5 that it was only in twelve of the total of 22 subjects tested that the largest amplitude was found in the measurements made in the morning (8 a.m.). In seven cases the largest

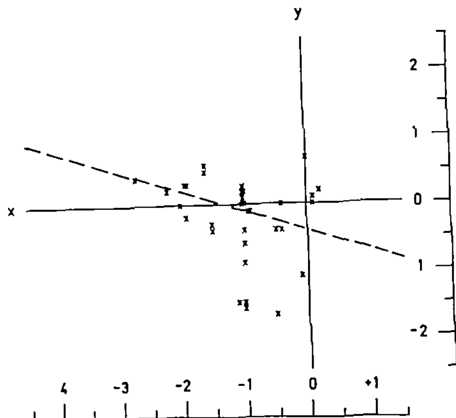


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The means (µV) and standard deviations of these results are presented in Fig. 6 The results obtained in the beginning of the experiment as well as after a period in the dark after stimulation with light and after a second period of dark-adaptation are shown. It is evident from this illustration that not only the average maximum amplitude (circles) obtained after 8 minutes of stimulation with light but also the decreased amplitude after both the first and the second 15-minute period of dark-adaptation (dots) as well as the amplitude obtained in the beginning of the experiment (dots) all show a slight continuous decrease during the course of the day The ratio of the maximum amplitude (after illumination, circles) to the minimum amplitude (after subsequent dark-adaptation) multiplied by a hundred ($\frac{\text{light peak}}{\text{dark trough}} \times 100$) remains fairly constant the values calculated from results obtained at 8 a.m 12 a.m 4 p.m. and 8 p.m. being 238 232 242 and 242 respectively The corresponding ratios calculated on the basis of measurements made after the first 15-minute period in the dark (before illumination) are 161 163 177 and 181 These ratios show a continuous increase in the course of the day the ratio obtained at 8 p.m. being 12.4 per cent larger than the ratio obtained at 8 a.m

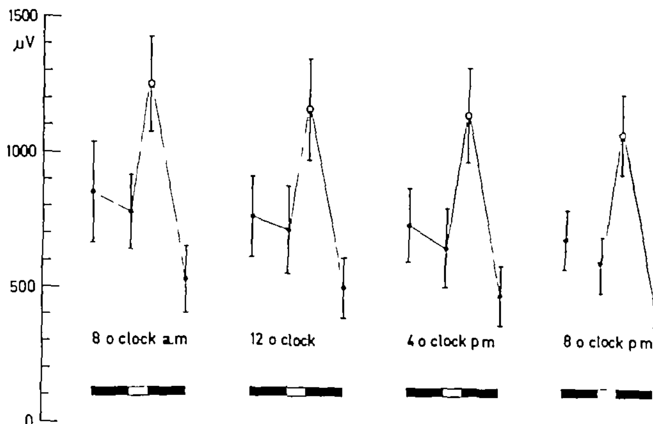


Fig. 6. Average amplitude (µV) of the EOG as measured in 22 subjects four times at four-hour intervals as indicated. Measurements were made at the beginning of the experiment (dots) and after the following periods: 15 minutes of preliminary dark-adaptation (dots), 8 minutes of illumination with light of 10 000 troland intensity (circles) and after a further 15-minute period of dark-adaptation (dots). Periods of darkness and illumination are marked on the abscissa with black and white respectively. Vertical bars indicate 2 × standard deviation.

that used in this laboratory for routine ENG recordings. However, in a part of the study on diurnal variation in the amplitude a D.C. differential amplifier and chlorinated silver electrodes were used. The light projected on to a white screen (80 × 80 cm square) placed 2 metres in front of the subject who was asked to look rhythmically between the two fixation lights, the eyes thus making horizontal excursions of 30 degrees. The measurements made in individual cases refer to the average amplitude obtained in a series of at least ten recordings of the EOG.

The diurnal variation in the amplitude of the EOG was investigated in 22 women aged 20 to 25. Each subject was examined four times (at 4-hour intervals) during one day, the hours of examination being 8 a.m., 12 a.m., 4 p.m. and 8 p.m. Table 5 shows the average results obtained after 8 minutes stimulation with light (10 000 troland, average diameter of the pupil 7 mm). It is evident that the average amplitude of the EOG decreases slightly in the course of the day. However, only the difference between the amplitude measured at 8 a.m. and 8 p.m. is statistically significant ($p < 0.001$), the average reduction in amplitude in this case being 13 per cent below the level measured in the morning. A statistically significant difference between the measurements made in the morning and in the evening was also found when measurements made after the first period in the dark ($p < 0.001$) or after the second period in the dark ($p < 0.01$) were used. It is also evident from Table 5 that it was only in twelve of the total of 22 subjects tested that the largest amplitude was found in the measurements made in the morning (8 a.m.). In seven cases the largest

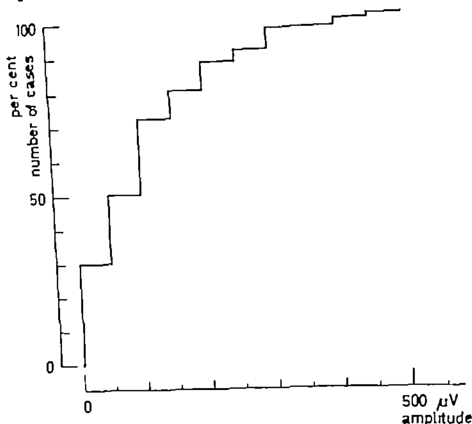


Fig. 8. Cumulative frequency histogram illustrating variation in the amplitude of the EOG as measured on two consecutive days. Abscissa, change in the amplitude as related to the amplitude measured 24 hours earlier (increase or decrease) in μV. Ordinate: percentage of measurements (total number of measurements = 278). All measurements were performed 8 minutes after the start of illumination with light of 1500 troland intensity.

cent (women) and 39 per cent (men) respectively. It is also evident that in some cases the amplitude increased, the largest increase observed in an individual case being 13 per cent (women) and 9 per cent (men) above the level measured in the morning respectively. However, the decrease in the amplitude observed in the data as a whole is statistically significant: t test value for women 9.4, $p < 0.001$ (at 58 degrees of freedom the t test value should be larger than 2.6 when $p < 0.001$) and correspondingly for men t test value 9.2, $p < 0.001$ (at 32 degrees of freedom the t test value should be larger than 2.7 when $p < 0.001$).

In a previous section of the present study it was shown that the velocity of the horizontal voluntary gaze movement does not show a measurable diurnal variation. This fact rules out the possibility that the results described above could have been due to attenuation in the R-C network of the amplified signal as a result of slowing down in the evening of the rise time of the input signal (velocity of eye movement).

Moreover, it was observed in the course of measurements of the velocity of horizontal gaze movement made with a D.C. amplifier that the amplitude of the EOG was larger in the morning than in the evening. This result was obtained with all ten subjects examined. To complete this study, similar measurements were made on twelve further subjects (5 women and 7 men, aged 20 to 25).

Chloridated silver electrodes and a D.C. differential amplifier were used and the procedure

Accordingly it is evident from Fig 6 that the dots representing the measurements made after 15 minutes in the dark before illumination (first dark trough) show approximately the same slope as the circles (measurements made after 8 minutes of illumination light peak) whereas the dots representing measurements made after 15 minutes in the dark after illumination (second dark trough) show a much less sloping course It is also evident from this illustration that the light induced increase in the amplitude of the EOG (from the first dark trough to the light peak) as expressed in absolute units (μV) remains fairly constant throughout the day This is supported by some further results presented below and obtained with 92 subjects examined at both 8 a.m and 8 p.m These results show that the average increase in the amplitude obtained in the morning is 410 μV as compared with 407 μV in the evening However further analysis of these results presented in Fig 7 indicates a negative correlation between the potential level measured before illumination (first dark trough) and the corresponding variation in the light induced fraction of the EOG This correlation is statistically significant ($p < 0.01$) The regression line calculated for these measurements can be expressed by the function $y = -0.426 - 0.293x$ coefficient of correlation -0.329

As mentioned above a statistically significant diurnal change in the amplitude of the EOG was observed only when the measurements made in the morning (8 a.m) were related to the measurements made in the evening (8 p.m) Therefore additional measurements made on 70 subjects were performed only in the morning and in the evening (the completed results thus including measurements made on 92 subjects 59 women and 33 men both aged 20 to 25) In 70 subjects the EOG was recorded at the beginning of the experiment after 15 minutes of dark-adaptation and after 8 minutes of illumination with light It was observed in five female subjects that the amplitude was larger in the evening than in the morning whereas in

Table 6 Results (obtained with 59 women) showing diurnal variation in the amplitude of the EOG recorded with the aid of a condenser-coupled differential amplifier The results show the relationship $\frac{A_1 - A_2}{A_1} \times 100$ (A_1 is the amplitude obtained at 8 a.m and A_2 is the amplitude obtained at 8 p.m.) Measurements were made after 8 minutes stimulation with light of 10 000 troland intensity following a 15-minute period of dark adaptation

Mean	12.7
Standard deviation	10.3
Maximum	31 4
Minimum	—13.8
Number of observations	59
t test value	9 4

the other females it decreased or was unaltered An increase in the amplitude was also observed in two of the men whereas in the others the amplitude decreased or was unaltered Mean values of the results (92 subjects) are presented in Table 6 (women) and Table 7 (men)

Tables 6 and 7 show the relationship $\frac{A_1 - A_2}{A_1}$ where A_1 is the amplitude obtained at 8 a.m and A_2 the amplitude obtained at 8 p.m. Multiplied by one hundred this relationship shows the relative alteration in the amplitude positive and negative results indicating a corresponding decrease or increase in the amplitude It is evident from these results that there is a mean decrease in the amplitude of 13 per cent in women (Table 6) and 18 per cent in men (Table 7) the maximal decrease in amplitude observed in an individual case being 31 per

Table 7 Results (obtained with 33 men) showing diurnal variation in the amplitude of the EOG recorded with the aid of a condenser-coupled differential amplifier The results show the relationship $\frac{A_1 - A_2}{A_1} \times 100$ (A_1 is the amplitude obtained at 8 a.m and A_2 is the amplitude obtained at 8 p.m) The measurement were made after 8 minutes of stimulation with light of 10 000 troland intensity following a 15-minute period of dark adaptation

Mean	18 4
Standard deviation	11 4
Maximum	39 5
Minimum	—9 7
Number of observations	33
t test value	9 4

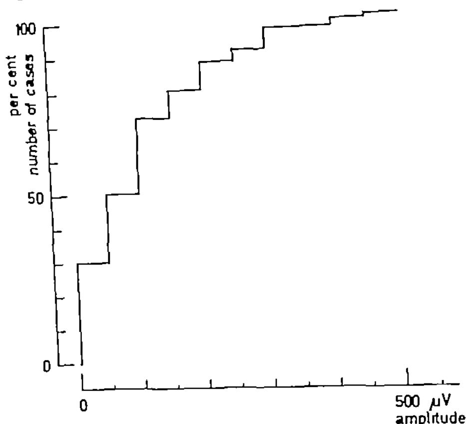


Fig. 8. Cumulative frequency histogram illustrating variation in the amplitude of the EOG as measured on two consecutive days. Abscissa, change in the amplitude as related to the amplitude measured 24 hours earlier (increase or decrease) in µV. Ordinate: percentage of measurements (total number of measurements = 278). All measurements were performed 8 minutes after the start of illumination with light of 1500 troland intensity.

cent (woman) and 39 per cent (man) respectively. It is also evident that in some cases the amplitude increased, the largest increase observed in an individual case being 13 per cent (woman) and 9 per cent (man) above the level measured in the morning respectively. However, the decrease in the amplitude observed in the data as a whole is statistically significant: t test value for women 9.4, $p < 0.001$ (at 58 degrees of freedom the t test value should be larger than 2.6 when $p < 0.001$) and correspondingly for men t test value 9.2, $p < 0.001$ (at 32 degrees of freedom the t test value should be larger than 2.7 when $p < 0.001$).

In a previous section of the present study it was shown that the velocity of the horizontal voluntary gaze movement does not show a measurable diurnal variation. This fact rules out the possibility that the results described above could have been due to attenuation in the R-C network of the amplified signal as a result of slowing down in the evening of the rise time of the input signal (velocity of eye movement).

Moreover, it was observed in the course of measurements of the velocity of horizontal gaze movement made with a D.C. amplifier that the amplitude of the EOG was larger in the morning than in the evening. This result was obtained with all ten subjects examined. To complete this study, similar measurements were made on twelve further subjects (5 women and 7 men, aged 20 to 25).

Chlorinated silver electrodes and a D.C. differential amplifier were used and the procedure

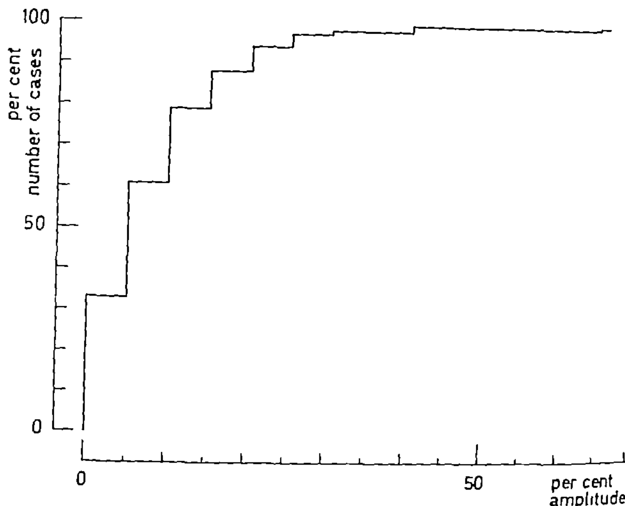


Fig 9 Cumulative frequency histogram illustrating variation (increase or decrease) in the amplitude of the EOG as measured on two consecutive days Abscissa change in the amplitude as a percentage of the amplitude measured 24 hours earlier Ordinate: percentage of measurements (total number of measurements = 278) All measurements were performed 8 minutes after the start of illumination with light of 1500 troland intensity

was in general the same as already described (p 13) However a somewhat slower velocity of the sweep (200 msec/cm) was used and automatic triggering was employed (in these subjects the velocity of the gaze movement was not measured)

Thus in a total of 22 subjects the amplitude of the EOG was measured (using D C amplification) both at 8 a.m and 8 p.m The recordings were made after 20 minutes of dark adaptation (no stimulation with light pupils not dilated) In 21 cases the smallest amplitude was found at 8 p.m whereas in one case no alteration of the amplitude was observed From the results obtained in the individual cases the relationship $\frac{A_1 - A_2}{A_1} \times 100$ (A_1 is the amplitude of the EOG measured at 8 a m and A_2 the amplitude measured at 8 p m) was calculated. These results are given in Table 8 The average reduction in the amplitude of the EOG is as high as 19 per cent the largest reduction in an individual case being 45 per cent below the amplitude measured in the morning Thet t test

Table 8 Decrease in amplitude of the EOG within a period of twelve hours (between 8 a.m. and 8 p.m.) expressed as a percentage of the amplitude measured at 8 a.m. The measurements were made on 22 subjects, using D.C. amplification.

Mean decrease in amplitude	19.3
Standard deviation	9.8
Maximum decrease	45.0
Minimum decrease	0.0
Number of observations	22
t test value	9.2

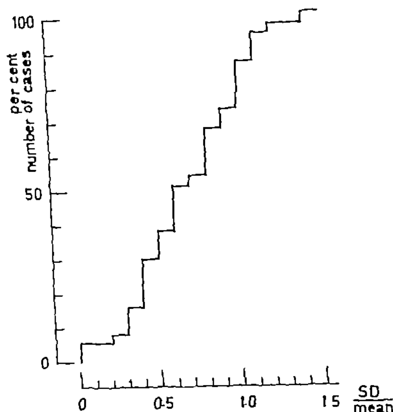


Fig. 10. Cumulative frequency histogram illustrating coefficient of variation of the change in the amplitude of the EOG. The results refer to measurements performed daily for period of 4 successive days. For each of the total of 37 series of measurements performed on 19 subjects, the mean and standard deviation of the 24-hour change in amplitude were calculated. Abscissa, SD/mean of the change in amplitude. Ordinate: percentage of measurements (total number of measurements = 37). All measurements were performed 8 minutes after the start of illumination with light of 1500 troland intensity.

value 9.2 indicates that the reduction in the amplitude in these subjects is statistically significant ($p < 0.001$).

To investigate variation in the amplitude of the EOG in the course of a period longer than twelve hours 25 subjects (women, aged 20 to 25) were examined several times in the course of the month. T exclude diurnal variation in the amplitude re-examination of the same subject was always performed at the same time of day. An attempt was made to examine every subject on as many consecutive days as possible; however for practical reasons the examinations had to be restricted to periods of four or three successive days. Examinations were performed with 19 subjects in a total of 37 periods of four days whereas on 6 subjects examinations were made in periods of three consecutive days only. Altogether 340 separate examinations were made. The EOG was recorded in the beginning of the experiment as well as after 15 minutes dark-adaptation and after 8 minutes stimulation with light of 1 500 troland intensity (pupils not dilated). The results described below refer to the amplitude obtained after stimulation with light.

From this material it was possible to collect 278 separate cases in which the EOG was recorded on two consecutive days (24-hour interval between recordings). The results are presented in the form of a cumulative frequency histogram (Fig. 8). In this histogram the change

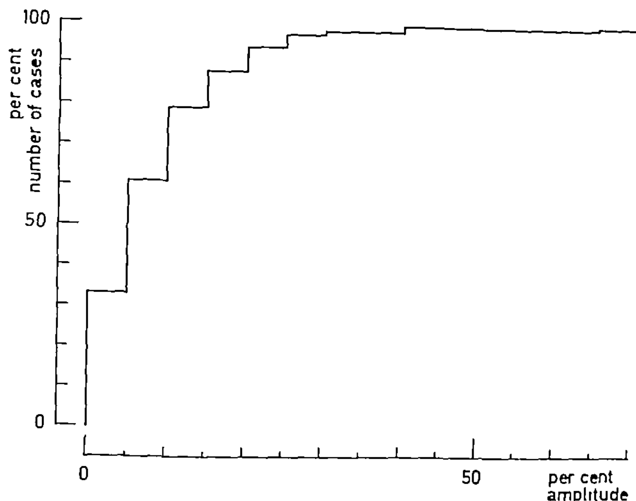


Fig 9 Cumulative frequency histogram illustrating variation (increase or decrease) in the amplitude of the EOG as measured on two consecutive days. Abscissa change in the amplitude as a percentage of the amplitude measured 24 hours earlier Ordinate percentage of measurements (total number of measurements = 278) All measurements were performed 8 minutes after the start of illumination with light of 1500 troland intensity

was in general the same as already described (p 13) However a somewhat slower velocity of the sweep (200 msec cm) was used and automatic triggering was employed (in these subjects the velocity of the gaze movement was not measured)

Thus in a total of 22 subjects the amplitude of the EOG was measured (using D C amplification) both at 8 a.m and 8 p m The recordings were made after 20 minutes of dark adaptation (no stimulation with light pupils not dilated) In 21 cases the smallest amplitude was found at 8 p.m whereas in one case no alteration of the amplitude was observed From the results obtained in the individual cases the relationship $\frac{A_1-A_2}{A_1} \times 100$ (A_1 is the amplitude of the EOG measured at 8 a m and A_2 the amplitude measured at 8 p.m) was calculated These results are given in Table 8 The average reduction in the amplitude of the EOG is as high as 19 per cent the largest reduction in an individual case being 45 per cent below the amplitude measured in the morning The t test

Table 8 Decrease in amplitude of the EOG within a period of twelve hours (between 8 a m. and 8 p.m) expressed as a percentage of the amplitude measured at 8 a.m. The measurements were made on 22 subjects, using D C. amplification

Mean decrease in amplitude	19 3
Standard deviation	9 8
Maximum decrease	45 0
Minimum decrease	0 0
Number of observations	22
t test value	9..

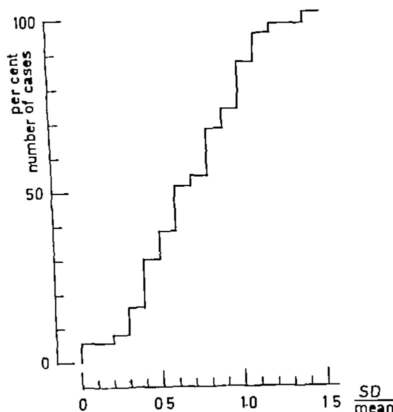


Fig 10 Cumulative frequency histogram illustrating coefficient of variation of the change in the amplitude of the EOG The results refer to measurements performed daily for period of 4 successive days. For each of the total of 37 series of measurements performed on 19 subjects, the mean and standard deviation of the 24-hour change in amplitude were calculated. Abscissa: SD/mean of the change in amplitude. Ordinate: percentage of measurements (total number of measurements = 37) All measurements were performed 8 minutes after the start of illumination with light of 1500 troland intensity

value 9 2 indicates that the reduction in the amplitude in these subjects is statistically significant ($p < 0\ 001$)

To investigate variation in the amplitude of the EOG in the course of a period longer than twelve hours, 25 subjects (women aged 20 to 25) were examined several times in the course of the month To exclude diurnal variation in the amplitude re-examination of the same subject was always performed at the same time of day An attempt was made to examine every subject on as many consecutive days as possible-however for practical reasons the examinations had to be restricted to periods of four or three successive days. Examinations were performed with 19 subjects in a total of 37 periods of four days whereas on 6 subjects examinations were made in periods of three consecutive days only Altogether 340 seperate examinations were made. The EOG was recorded in the beginning of the experiment as well as after 15 minutes dark-adaptation and after 8 minutes stimulation with light of 1 500 troland intensity (pupils not dilated) The results described below refer to the amplitude obtained after stimulation with light.

From this material it was possible to collect 278 separate cases in which the EOG was recorded on two consecutive days (24-hour interval between recordings) The results are presented in the form of a cumulative frequency histogram (Fig 8) In this histogram the change

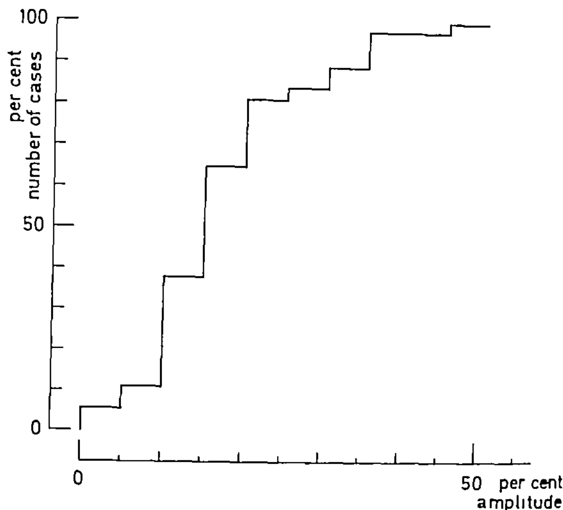


Fig 11 Cumulative frequency histogram illustrating variation in the amplitude of the EOG as measured daily for a period of four successive days. Abscissa difference between the largest and the smallest amplitude as a percentage of the smallest amplitude observed Ordinate, percentage of measurements (total number of measurements = 37) (37 periods each 4 days, 19 subjects) All measurements were performed 8 minutes after the start of illumination with light of 1500 troland intensity

(increase and decrease) in the amplitude in relation to the value measured 24 hours earlier (abscissa) is shown as a function of the percentage of measurements (total number of measurements = 278 ordinate) It is evident from this illustration that in 50 per cent of cases the change in the amplitude is less than 100 μV in 80 per cent of cases less than 200 μV and in 100 per cent of cases less than 500 μV The same results are presented in Fig 9 to show the change in amplitude (increase or decrease) as a percentage of the amplitude found 24 hours earlier This histogram shows that in 60 per cent of cases the change in amplitude is less than 10 per cent and in most cases (more than 90 per cent) less than 20 per cent

To investigate variation in the change of amplitude of the EOG recorded at 24-hour intervals the mean and standard deviation of the change in amplitude (increase or decrease within 24 hours) was calculated from results obtained with 19 subjects (37 periods of measurements performed on four successive days) The results are presented in the form of cumulative frequency histogram (Fig 10) showing the coefficient of variation of the change in amplitude as a function of the percentage of measurements (total number of measurements = 37) It is evident from this illustration that in about 70 per cent of the cases (total 37) the coefficient of variation is larger than 0 5 In these cases the standard

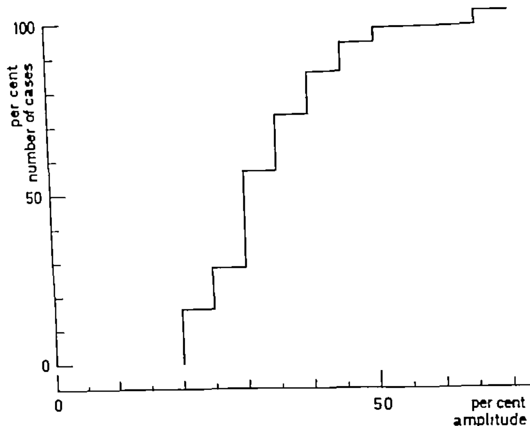


Fig 12. Cumulative frequency histogram illustrating variation in the amplitude of the EOG as measured on 25 subjects on several occasions for period of one month (340 separate measurements) Abscissa, difference between the largest and the smallest amplitude as percentage of the smallest amplitude. Ordinate percentage of measurements (total number of measurements = 25) All measurements were performed 8 minutes after the start of illumination with light of 1300 troland intensity

deviation is larger than 50 per cent of the average change in the amplitude indicating a large variation in the change of the amplitude observed within 24 hours.

In the same set of experimental data consisting of 37 periods of measurements performed on four successive days the relationship $\frac{A_1-A_2}{A_2} \times 100$ was calculated (A_1 is the largest amplitude and A_2 the smallest amplitude observed) The results are presented as a cumulative frequency histogram (Fig 11) This histogram shows the difference between the largest and smallest amplitude (obtained within four days) expressed as a percentage of the smallest amplitude observed (abscissa) as a function of the percentage of measurements (total number of measurements = 37 ordinate) It is evident from this illustration that in 10 per cent of cases the difference between the largest and the smallest amplitude is less than 10 per cent and in about 60 per cent of cases the difference is less than 20 per cent In 11 per cent of cases the difference exceeds 35 per cent and only in one case is there a 50 per cent difference between the largest and the smallest amplitude obtained within a period of four successive days

To investigate variation in the amplitude of the EOG in the course of one month the relationship $\frac{A_1-A_2}{A_2} \times 100$ (where A_1 is the largest and A_2 the smallest amplitude obtained) was

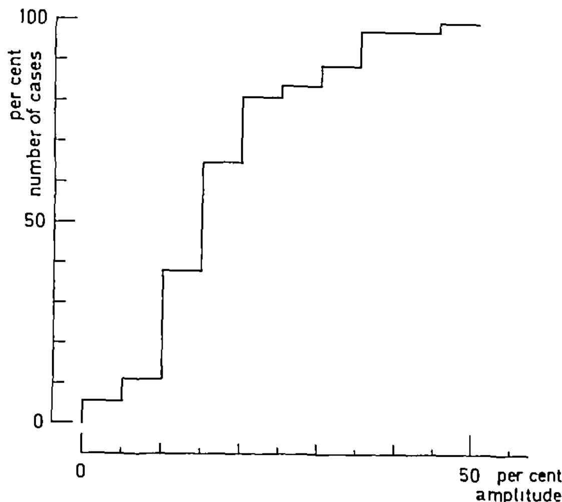


Fig. 11 Cumulative frequency histogram illustrating variation in the amplitude of the EOG as measured daily for a period of four successive days. Abscissa, difference between the largest and the smallest amplitude as a percentage of the smallest amplitude observed. Ordinate, percentage of measurements (total number of measurements = 37) (37 periods each 4 days 19 subjects) All measurements were performed 8 minutes after the start of illumination with light of 1500 troland intensity

(increase and decrease) in the amplitude in relation to the value measured 24 hours earlier (abscissa) is shown as a function of the percentage of measurements (total number of measurements = 278 ordinate) It is evident from this illustration that in 50 per cent of cases the change in the amplitude is less than 100 μV in 80 per cent of cases less than 200 μV and in 100 per cent of cases less than 500 μV The same results are presented in Fig 9 to show the change in amplitude (increase or decrease) as a percentage of the amplitude found 24 hours earlier This histogram shows that in 60 per cent of cases the change in amplitude is less than 10 per cent and in most cases (more than 90 per cent) less than 20 per cent

To investigate variation in the change of amplitude of the EOG recorded at 24-hour intervals the mean and standard deviation of the change in amplitude (increase or decrease within 24 hours) was calculated from results obtained with 19 subjects (37 periods of measurements performed on four successive days) The results are presented in the form of cumulative frequency histogram (Fig 10) showing the coefficient of variation of the change in amplitude as a function of the percentage of measurements (total number of measurements = 37) It is evident from this illustration that in about 70 per cent of the cases (total 37) the coefficient of variation is larger than 0 5 In these cases the standard

Table 9 Amplitude of the EOG (mm, 1 mm refers to 125 μV) as measured on 9 subjects at four-weekly intervals during 10 months. Mean amplitude, standard deviation, maximum and minimum amplitudes, number of observations, as well as t test values for the different months are shown. All measurements were performed 8 minutes after stimulation with light of 10 000 troland intensity

Mean		9.7
Standard deviation		2.0
Maximum		13.9
Minimum		6 0
Number of observations		90
t test value	May	—0 0273
	July	0.9841
	August	0.3436
	September	0.3855
	October	0 2699
	November	—1.0348
	December	—1 8626
	January	—1.2423
	February	0 1030
	March	1.1701

intervals for ten months was compared to the mean amplitudes obtained for these subjects for each of the ten separate months The results are shown in Table 9 The t test values show very little difference between the average results obtained in different months and the averaged results for the whole ten-month period.

From results obtained with 20 subjects the relationship $\frac{A_1 - A_2}{A_2} \times 100$ was calculated (A is the largest amplitude and A_2 is the smallest) The results are presented in the form of a cumulative frequency histogram (Fig. 13) In this histogram the difference between the largest and the smallest amplitude observed within ten months is presented as a percentage of the smallest amplitude (abscissa) and is shown as a function of the percentage of measurements (total number of measurements = 20 ordinate) In all test subjects the difference between the largest and the smallest amplitude was greater than 20 per cent In 80 per cent of cases the difference was less than 50 per cent and in 100 per cent of cases the difference was less than 70 per cent of the smallest amplitude.

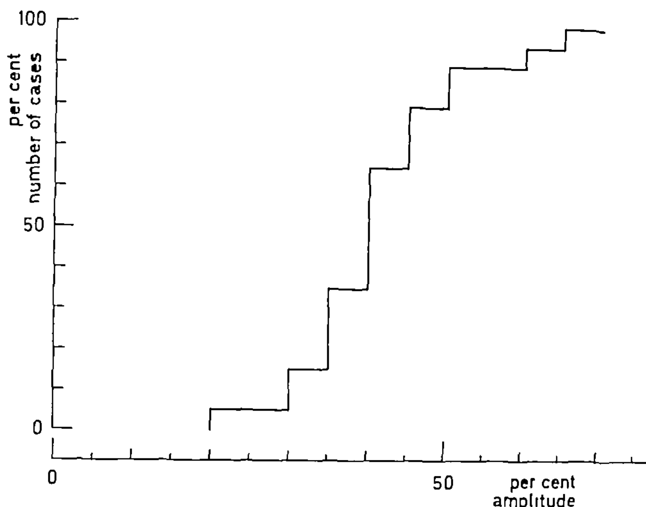


Fig 13 Cumulative frequency histogram illustrating variation in the amplitude of the EOG as measured on 20 subjects for a period of ten months (194 separate measurements) Abscissa difference between the largest and the smallest amplitude as a percentage of the smallest amplitude. Ordinate percentage of measurements (total number of measurements = 20) *All measurements were performed 8 minutes after the beginning of illumination* with light of 10 000 troland intensity

calculated for the results obtained in all 25 subjects examined (340 separate measurements) The results are presented in the form of a cumulative frequency histogram (Fig 12) *The histogram shows the difference between the* largest and smallest amplitudes (obtained within one month) expressed as a percentage of the smallest amplitude (abscissa) as a function of the percentage of measurements (total number of measurements = 25 ordinate) It is evident from this illustration that in all the subjects the difference between the largest and smallest amplitude is larger than 20 per cent On the other hand in about 55 per cent of cases the difference is less than 30 per cent and in about 90 per cent of cases the difference between the largest and smallest amplitudes is less than 50 per cent of the smallest amplitude

The investigation of spontaneous variation in the amplitude of the EOG was completed with *a study extending over ten months* These measurements were made on 20 women aged 20 to 25 However in the course of time the number fell and only 9 of these subjects attended all examinations All experiments were performed at the same time of day (8 a m) and repeated at four weekly intervals The recordings were made after 8 minutes of stimulation with light of 10 000 troland intensity (pupils dilated) *following a 15-minute period of dark adaptation*

The mean amplitude for the nine subjects obtained from the EOGs performed at monthly

Table 9 Amplitude of the EOG (mm, 1 mm refers to 125 μV) as measured on 9 subjects at four-weekly intervals during 10 months. Mean amplitude standard deviation, maximum and minimum amplitudes number of observations, as well as t test values for the different months are shown. All measurements were performed 8 minutes after stimulation with light of 10 000 troland intensity

Mean		9.7
Standard deviation		2.0
Maximum		13.9
Minimum		6.0
Number of observations		90
t test value	May	−0 0273
	July	0.9841
	August	0.3436
	September	0.3855
	October	0.2699
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	January	−1.2423
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intervals for ten months was compared to the mean amplitudes obtained for these subjects for each of the ten separate months The results are shown in Table 9 The t test values show very little difference between the average results obtained in different months and the averaged results for the whole ten-month period.

From results obtained with 20 subjects the relationship $\frac{A_1-A_2}{A_2} \times 100$ was calculated (A_1 is the largest amplitude and A_2 is the smallest) The results are presented in the form of a cumulative frequency histogram (Fig. 13) In this histogram the difference between the largest and the smallest amplitude observed within ten months is presented as a percentage of the smallest amplitude (abscissa) and is shown as a function of the percentage of measurements (total number of measurements = 20 ordinate) In all test subjects the difference between the largest and the smallest amplitude was greater than 20 per cent, in 80 per cent of cases the difference was less than 50 per cent and in 100 per cent of cases the difference was less than 70 per cent of the smallest amplitude.

V Discussion

It was confirmed in a series of preliminary experiments that small displacements of the two recording electrodes located on the skin near the temporal canthi of the lids of both eyes do not very much influence the recorded amplitude of the EOG An average increase in the inter electrode distance of more than 10 mm was required to decrease the amplitude of the EOG by an average of 10 per cent In the present study markings made with ink on the skin greatly facilitated the positioning of the elec trodes in cases where a second test was made within 24 hours When the re-examination was made after a longer period of time the only way to check the location was to place the elec trodes as near the temporal canthi of the lids as possible without causing excess of tear fluid at the skin electrode contact

In another series of preliminary experiments it was observed that a lamp consisting of three fluorescent tubes mounted in the ceiling and used as part of the standard illumination of the routine ENG laboratory was strong enough to produce a considerable increase in the amplitude of the EOG previously measured in the dark adapted eye (Fig 3) In most of the experi ments of the present study however a standard light source was used to provide the illumination used for stimulation The light was projected on a white screen in front of the subject to be examined and the average intensity of light was calculated to be 10 000 photopic troland (pupils dilated) and 1 500 photopic troland (pupils not dilated) The pupils were not dilated in cases where the experiments were repeated on several successive days because of the in- convenience to the test subject of prolonged mydriasis and paresis of accommodation. It should be noted that in the present experiments only a central part of the retina was directly illuminated by the stimulating light the pe ripheral retina being illuminated by stray light. It is also known that the amplitude of the EOG, measured after a constant period of illumination, is linearly related to the logarithm of the inten sity of the light used for stimulation (Heck and Papst 1957) In the human eye an in crease in the energy of the illumination above an average of 10 000 troland is not related to any further increase in amplitude (Arden and Kelsey 1962 b)

The results of the present work show that the increase in the amplitude provoked by the standard illumination (36 test subjects Fig 5) is on the average 45 per cent above the level measured at the beginning of the experiment. This of course is sufficient to produce a con siderable improvement in the signal-to-noise ratio of routine clinical recordings Simulta neously with the increase in the amplitude the variation in the amplitude shows a statistically significant decrease the coefficient of variation calculated from results obtained 8 minutes after stimulation with light being 0 165 as compared with 0.266 0.251 and 0 270 for the results obtained at the beginning of the experiment and after the first and second 15 minute periods of dark-adaptation respectively A larger number of data collected from experiments performed at different times of day (Table 4 92 subjects, 184 measurements) shows that at the beginning of the experiment when the average amplitude of the EOG is 660 μV the coefficient of varia tion is 0 309 whereas after 8 minutes of illu mination with light of 10 000 troland inten sity the amplitude is increased to an average of 1025 μV and the coefficient of variation is reduced to 0.252 This result was statistically significant $p < 0\ 01$ It is also evident (Fig 4) that the absolute value of the standard deviation

is smaller after illumination than at the beginning of the experiment and almost as large as after the first 15-minute period in the dark. In addition, it was established (Figs. 4 and 6) that after the second 15-minute period of dark adaptation the amplitude of the EOG is smaller than after the first period in the dark. This is in agreement with the results of ASERINSKY (1955) who found that when the eye was exposed to several periods of light and darkness the amplitude of the EOG was further reduced during every successive dark period until finally a constant level was reached. This is not apparent in the results of ARDEN and KELSEY (1962 a)

To achieve a constant base-line value of the EOG response, a long period of steady illumination or darkness is required (KOLDER, 1959) This fact complicates the results of the present study A preliminary 15-minute period of dark adaptation is too short to achieve a constant base-line. After illumination, on the other hand, the minimum level of the dark trough has already been passed and the potential increases again if only a single measurement is made at the end of a 15-minute period in the dark. Moreover during the first 15-minute period in the dark at the beginning of the experiment it was observed that in individual cases the amplitude remained unaltered or showed a slight decrease or even an increase. Stimulation with light synchronizes the oscillations of the potential. The fact that the variation coefficient calculated for the amplitude obtained after the second period in the dark is as large as the coefficient obtained after the first period in the dark and larger than the coefficient obtained after an 8-minute period of illumination apparently indicates reduction in the accuracy of the measurements due to the strongly reduced amplitude of the response at the end of the second period in the dark The constant 15-minute duration of the dark period used in the present study was originally chosen as a compromise between the favourable effects of a long period of dark-adaptation on the subsequent light induced increase in the amplitude of the EOG (ARDEN and KELSEY 1962 a) and the inconvenience to the test subject of an experiment of long total duration.

In the present work a statistically significant diurnal alteration in the amplitude of the EOG was observed both in the measurements made after a preliminary 15-minute period in the dark and after a period of light-adaptation of 8 minutes duration. The measurements made after the second 15-minute period in the dark showed much less alteration the diurnal variation in this case being statistically significant, $p < 0.01$ The results obtained after 8 minutes illumination showed that the average decrease in the amplitude of the EOG between 8 a.m and 8 p.m. was 12.7 per cent (59 women Table 6) and 18.4 per cent (33 men, Table 7) In addition, it was confirmed in a series of experiments performed with a D.C. amplifier that the diurnal alteration in the amplitude of the EOG is not due to a diurnal variation in the velocity of the horizontal eye movements. It is also known that the velocity of a gaze movement cannot be altered by voluntary effort (BROCKHURST and LION 1951 MACKENSEN 1958) In agreement with the results described above these measurements (performed on 22 test subjects using D.C. amplification) showed that the amplitude measured at 8 p.m. was on the average 19.3 per cent smaller than the amplitude measured at 8 a.m. Slowing down of the velocity of the voluntary gaze movement may occur in physical and mental fatigue (DODGE and CLINE, 1901 MILES 1929) KRIS (1960) found a remarkably low average velocity (100°/sec) of the horizontal eye movement in subjects examined early in the morning as compared with subjects examined in the afternoon (350°/sec) However only a totally reversed difference in the velocity of the eye movement (observed in the morning and in the afternoon) could be related to the largely increased amplitude of the EOG in the afternoon as observed by KRIS (1960)

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V Discussion

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crease in the amplitude of the EOG probably being initiated in the receptors (see Introduction) The nature of the processes leading to diurnal variation in the activity of the pigment epithelium is not known However in many other organs with great metabolic activity the circadian rhythm in the activity (MILLS 1966) parallels the slow diurnal variation in the blood level of the corticosteroid hormones (PETERSON 1957) In the human eye the effects of the corticosteroid hormones on intraocular pressure are well known

In the present study spontaneous variations in the amplitude of the EOG were also investigated in the course of longer periods by making re-examinations at 24-hour intervals as well as at monthly intervals In these experiments too stimulation with light was used to increase and stabilize the amplitude of the EOG and all experiments performed on the same test subject were made at the same time of day to avoid diurnal variation.

In 278 cases the amplitude of the EOG was measured on two consecutive days (24-hour interval between recordings) It was observed that in 60 per cent of cases the change in the amplitude (increase or decrease) was less than 10 per cent and in most cases (more than 90 per cent) it was less than 20 per cent (Fig 9)

It was also of interest to know about the variation in the amplitude of the EOG recorded in the same subject on several consecutive days (24-hour interval between recordings) In 19 subjects such measurements were performed on four consecutive days (37 periods of measurements each of four day duration) It was found that the coefficient of variation (SD mean) of the change in the amplitude (increase or decrease within 24 hours) was larger than 0 5 in about 70 per cent of cases indicating a great variation in the change of the amplitude within three successive 24-hour periods (Fig. 10) From the same experimental data obtained in 19 subjects (37 periods of measurements of four days duration) it was calculated that in 10 per cent of cases the difference between the largest and the smallest amplitude was less than 10 per cent, and in about 60 per cent of cases it was less than 20 per cent. Only in a very few cases was there a difference of as much as 50 per cent between the largest and the smallest amplitude obtained within three consecutive 24-hour periods (Fig. 11) Apparently the relative difference between the largest and the smallest amplitude of the EOG increases with the length of the period between recordings Measurements made on the same subject at monthly intervals showed (Fig. 12 25 subjects 340 measurements) that in this case this difference was larger than 20 per cent in all test subjects and in about 90 per cent of cases the difference was less than 50 per cent of the smallest amplitude. Only in nine test subjects could the measurements made at monthly intervals be continued for a period of ten months But in this series of measurements also the difference between the smallest and the largest amplitude was greater than 20 per cent in all test subjects, whereas in 80 per cent of cases the difference was less than 50 per cent and in all cases the difference was less than 70 per cent of the smallest amplitude.

It can be concluded that substantial spontaneous variations occur in the amplitude of the EOG of healthy eyes In most cases the amplitude shows a slow decrease from morning to night, whereas the changes observed over longer periods (24 hours 4 days 1 month and 10 months) show no regular pattern Even after a month or ten months there were a few cases (10 to 20 per cent of the total number) in which the changes exceeded 50 per cent of the smallest amplitude observed, the change observed within 24 hours being of lesser magnitude. On the other hand, the changes observed within one month to ten months were in all cases larger than 20 per cent of the minimum amplitude. Day to day changes in the amplitude of the b-wave of the human ERG examined by SPIVEY and PEARLMAN (1963) in 19 young normal subjects varied from 16 to 95 per cent the difference between the largest and the

tude of the EOG observed in the present study is not likely to be related to a change in the skin-electrode resistance. Measurements performed on a large number of subjects (page 10) showed no difference in the average skin electrode resistance obtained in the morning and in the afternoon respectively. However, the average age of these subjects was high as compared with the subjects of the main experiments of the present study. In two subjects (aged 22 and 26) RUTENFRANZ (1955) examined the diurnal variation of the electrical resistance of the skin on the palmar side of the wrist and found a maximum at 9 a.m., a minimum at 1 p.m. and another equally large maximum at 7 p.m. Apparently, this type of variation in the electrical resistance of the skin is not synchronous with the continuous slow diurnal variation in the amplitude of the EOG described above. SHACKEL (1959) eroded the skin to reduce the electrical resistance at the site of the electrodes in their recordings of the human EOG. This procedure called "skin drilling" was not applied to the present study because of the complications caused to the skin as a result of experiments repeated at short intervals by using the same position of the electrodes.

The average results obtained in another group of 22 test subjects (Fig. 6) indicate that the light induced fraction of the amplitude of the EOG (the amplitude measured between the level obtained after a preliminary 15-minute period in the dark and the level obtained at the end of 8 minutes illumination does not show diurnal variation, and the average light induced fraction of the results obtained in 92 test subjects at 8 a.m. (410 μV) equaled that obtained in the same subjects at 8 p.m. (407 μV). However, there are wide variations between individuals. The relationship between the diurnal alteration (8 a.m. to 8 p.m.) in the light-induced fraction of the EOG and the corresponding diurnal alteration in the amplitude measured at the end of the preliminary 15 minute period of dark-adaptation (Fig. 7) shows that in most individual cases the amplitude measured at the end of the preliminary period in the dark decreased in the course of the day, whereas there was an almost equal number of cases showing an increase or a decrease in the light induced fraction of the EOG. This illustration also suggests that in cases with a large diurnal reduction in the amplitude as measured after 15 minutes in the dark, the corresponding light induced fraction of the EOG is likely to show an increase. On the contrary, in those cases with a small diurnal reduction in the amplitude level obtained at the end of the 15 minute period in the dark, the corresponding light induced fraction of the EOG is likely to remain unaltered or to show a diurnal decrease. This is expressed by the negative correlation between these two processes illustrated in Fig. 7 by the interrupted line.

ASERINSKY (1955), when studying the effects of sleep on the amplitude of the EOG, found that the amplitude measured early in the morning was larger than the amplitude measured in the same subjects the previous evening. This is in apparent agreement with the slow reduction in the amplitude of the EOG during the course of the day observed in most subjects examined in the present study. The amplitude was only found to increase in a minority of cases and in these cases the increase was small as compared with that (doupled or trebled amplitude) described by KRIS (1960). The slow decrease in the amplitude of the EOG in the course of the day resembles the diurnal variation in the amplitude of the b-wave of the human electroretinogram (ERG) described by RONCHI and ERCOLES (1967). On the other hand, in the monkey eye there seems to be a simple linear relationship between the amplitude of the EOG and the amplitude of the ERG (GOURAS and CARR 1964). In the human eye and in the eye of the rabbit SPIVEY and PEARLMAN (1963) have observed considerably day to day variations in the amplitude of ERG.

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smallest amplitude being expressed in per cent of the smallest Excluding three extreme cases this variation was from 16 to 45 per cent In the present study the change in the amplitude of the EOG obtained within 24 hours was expressed in per cent of the first measurement (made 24 hours earlier) this change being less than 10 per cent in 60 per cent of cases and less than 20 per cent in 90 per cent of cases These results are not directly comparable with earlier reports The results of DAVIS and SHACKEL (1960) are presented in absolute units (μV) only moreover there are fundamental differences in the recording procedures They found that in twelve healthy young subjects the average change in the amplitude was 76 μV within 24 hours (30 degree excursion of the eyes) this change being larger than 200 μV in 6 per cent of cases and larger than 100 μV in 25 per cent of cases Correspondingly in the present study the change in the amplitude was larger than 200 μV in 20 per cent of cases and larger than 100 μV in 50 per cent of cases In the results of DAVIS and SHACKEL (1960) the time between the recordings (1 hour 24 hours 8 weeks) did not alter the results very much and there was no definite diurnal pattern of variation

The clinical evaluation of the intensity of spontaneous nystagmus is based on measurements of the maximal velocity of the slow phase of the nystagmus Accordingly the velocity of the slow phase of the nystagmus observed during the maximal intensity of the caloric nystagmus is the best indicator of the caloric excitability of the labyrinthine organ On the other hand the total (summed) amplitude of the nystagmus observed during the caloric reaction provides a reliable indicator of the excitability (ASCHAN BERGSTEDT and STAHLE, 1956, HENRIKSSON 1956) In the clinical procedures of recording the nystagmus the subject is occasionally asked to close his eyes or to keep them open Thus the fact that light and darkness alter the amplitude of the corneo-fundal potential indicates the necessity of measuring the illumination in the ENG laboratory Moreover it is important to make frequent calibrations of the amplitude by asking the subject to perform horizontal gaze movements through a constant angle The favourable effect of a long period of preliminary dark-adaptation for the clinical ENG recording has already been emphasized by MUNTHE FOG (1963) On the other hand as mentioned above it is difficult to achieve a steady base-line level (KOLDER 1959) Even short periods of light start the slow oscillatory alteration in the amplitude of the corneo-fundal potential (ARDEN and KELSEY 1962a) However to obtain a maximum increase in the amplitude it is necessary to use a longer period of continuous illumination following a constant period in the dark and to perform the recordings 8 to 10 minutes after the beginning of the illumination This procedure not only facilitates the detection of nystagmus of limited amplitude (ELENIUS and AANTAA 1967) but also markedly improves the signal-to-noise ratio of the recordings In the present work the use of a light induced increase in the amplitude of the corneo-fundal potential made it possible to use relatively low amplification (1250 μV cm) and the quality of the recordings was good The use of higher amplification in the present study was limited by the restricted maximal vertical excursion (20 mm) of the pen recorder of the electro-nystagmograph used

Summary

When recording the electro-oculogram (EOG) with the aid of a condenser-coupled differential amplifier and two electrodes placed on the skin near the temporal canthi of the lids of both eyes, it was found, that a lateral displacement of one or both electrodes reduced the amplitude of the EOG an increase in the inter-electrode distance of 10 mm corresponding to a 10 per cent average reduction in the amplitude. In the original (primary) position the nearest edge of the electrodes was 14 mm from the canthus of the lids. The EOG was evoked by moving the eyes horizontally from one fixation light to the other (through a constant angle)

The effect of illumination on the amplitude of the EOG was first investigated after 30 minutes of dark-adaptation by switching on the standard illumination (1000 troland) of the examination room. This light increased the amplitude in 8 minutes (20 subjects) on the average by 39 per cent above the level obtained at the beginning of the experiment.

The effect of stronger illumination (10 000 troland) was investigated with the aid of a Leitz projector by switching on the light after 15 minutes of dark-adaptation. It was found that in 8 minutes this light increased the amplitude by an average (36 subjects) of 45 per cent above the level obtained at the beginning of the experiment It was also found that the variation in the amplitude was smaller after 8 minutes of illumination (large amplitude) than at the beginning of the experiment.

The diurnal variation in the amplitude of the EOG was investigated by performing the experiments after 8 minutes of light-adaptation (10 000 troland) following a 15-minute period of dark-adaptation Measurements were performed at 8 a.m. 12 a.m., 4 p.m., and 8 p.m. A slow diurnal reduction between 8 a.m and 8 p.m. was found, the difference between the values being statistically significant ($p < 0.001$) The magnitude of the reduction was on the average 12.7 per cent (59 women) and 18.4 per cent (33 men)

Diurnal variation in the amplitude of the EOG was also found in control experiments made using a D.C. differential amplifier the corresponding average reduction in the amplitude in this series of experiments (22 subjects) being 19.3 per cent. In addition, it was found (by using D.C. amplification) that the velocity of the voluntary horizontal gaze movement does not show diurnal variation.

The average light-induced fraction of the EOG (measured from the level obtained after 15 minutes in the dark before illumination to the level obtained 8 minutes after the beginning of illumination) was found to be the same (92 subjects) at 8 a.m. as at 8 p.m. Individual cases however showed a slight negative correlation (coefficient of correlation —0.329) between the amplitude obtained after 15 minutes in the dark and the light-induced fraction of the EOG

In 278 cases the amplitude of the EOG was measured on two consecutive days (24-hour interval between recordings) It was observed that in 60 per cent of these cases the change in the amplitude (increase or decrease) was less than 10 per cent and in most cases (more than 90 per cent) it was less than 20 per cent.

In 19 subjects (37 periods of measurements each of four days duration) it was calculated that in 10 per cent of cases the difference between the largest and the smallest amplitude was less than 10 per cent and in about 60 per cent of cases it was less than 20 per cent. Only in a very few cases was there a difference of as much as 50 per cent between the largest

smallest amplitude being expressed in per cent of the smallest. Excluding three extreme cases this variation was from 16 to 45 per cent. In the present study the change in the amplitude of the EOG obtained within 24 hours was expressed in per cent of the first measurement (made 24 hours earlier) this change being less than 10 per cent in 60 per cent of cases *and less than 20 per cent in 90* per cent of cases These results are not directly comparable with earlier reports The results of DAVIS and SHACKEL (1960) are presented in absolute units (µV) only *moreover there are fundamental* differences in the recording procedures. They found that in twelve healthy young subjects the average change in the amplitude was 76 µV within 24 hours (30 degree excursion of the eyes) this change being larger than 200 µV in 6 per cent of cases and larger than 100 µV in 25 per cent of cases. Correspondingly in the present study the change in the amplitude was larger than 200 µV in 20 per cent of cases and larger than 100 µV in 50 per cent of cases In the results of DAVIS and SHACKEL *(1960)* the time between the recordings (1 hour 24 hours 8 weeks) *did not* alter the results very *much and* there was no definite diurnal pattern of variation

The clinical evaluation of the intensity of spontaneous nystagmus is based on measurements of the maximal velocity of the slow phase of the nystagmus Accordingly the velocity of the slow phase of the nystagmus observed during the maximal intensity of the caloric nystagmus is the best indicator of the caloric excitability of the labyrinthine organ. On the other hand the total (summed) amplitude of the nystagmus observed during the caloric reaction provides a reliable indicator of the excitability (ASCHAN BERGSTEDT and STAHLE 1956 HENRIKSSON 1956) In the clinical procedures of recording the nystagmus, the subject is occasionally asked to close his eyes or to keep them open. Thus the fact that light and darkness alter the amplitude of the corneo-fundal potential indicates the necessity of measuring the illumination in the ENG laboratory Moreover it is important to make frequent calibrations of the amplitude by asking the subject to perform *horizontal gaze movements through a constant* angle. The favourable effect of a long period *of preliminary dark adaptation for the clinical* ENG recording has already been emphasized by MUNTHE FOG (1963) On the other hand as mentioned above it is difficult to achieve a steady base-line level (KOLDER 1959) Even short periods of light start the slow oscillatory alteration in the amplitude of the corneo-fundal potential (ARDEN and KELSEY 1962a) However to obtain a maximum increase in the amplitude it is necessary to use a longer period of continuous illumination following a constant period in the dark, and to perform the recordings 8 to 10 minutes after the beginning of the *illumination This procedure not only* facilitates the detection of nystagmus of limited amplitude (ELENIUS and AANTAA 1967) but also markedly improves the signal-to-noise ratio of the recordings In the present work the use of a light induced increase in the amplitude of the corneo-fundal potential made it possible to use relatively low amplification (1250 µV cm) and the quality of the recordings was good The use of higher amplification in the present study was limited by the restricted maximal vertical excursion (*20* mm) of the pen recorder of the electro-nystagmograph used.

Summary

When recording the electro-oculogram (EOG) with the aid of a condenser-coupled differential amplifier and two electrodes placed on the skin near the temporal canthi of the lids of both eyes, it was found, that a lateral displacement of one or both electrodes reduced the amplitude of the EOG an increase in the inter-electrode distance of 10 mm corresponding to a 10 per cent average reduction in the amplitude. In the original (primary) position the nearest edge of the electrodes was 14 mm from the canthus of the lids. The EOG was evoked by moving the eyes horizontally from one fixation light to the other (through a constant angle)

The effect of illumination on the amplitude of the EOG was first investigated after 30 minutes of dark-adaptation by switching on the standard illumination (1000 troland) of the examination room. This light increased the amplitude in 8 minutes (20 subjects) on the average by 39 per cent above the level obtained at the beginning of the experiment

The effect of stronger illumination (10 000 troland) was investigated with the aid of a Leitz projector by switching on the light after 15 minutes of dark-adaptation It was found that in 8 minutes this light increased the amplitude by an average (36 subjects) of 45 per cent above the level obtained at the beginning of the experiment It was also found that the variation in the amplitude was smaller after 8 minutes of illumination (large amplitude) than at the beginning of the experiment.

The diurnal variation in the amplitude of the EOG was investigated by performing the experiments after 8 minutes of light-adaptation (10 000 troland) following a 15-minute period of dark-adaptation. Measurements were performed at 8 a.m. 12 a.m., 4 p.m. and 8 p.m. A slow diurnal reduction between 8 a.m and 8 p.m was found, the difference between the values being statistically significant ($p < 0.001$) The magnitude of the reduction was on the average 12.7 per cent (59 women) and 18.4 per cent (33 men)

Diurnal variation in the amplitude of the EOG was also found in control experiments made using a D.C. differential amplifier the corresponding average reduction in the amplitude in this series of experiments (22 subjects) being 19.3 per cent. In addition, it was found (by using D.C. amplification) that the velocity of the voluntary horizontal gaze movement does not show diurnal variation.

The average light-induced fraction of the EOG (measured from the level obtained after 15 minutes in the dark before illumination to the level obtained 8 minutes after the beginning of illumination) was found to be the same (92 subjects) at 8 a.m. as at 8 p.m Individual cases, however showed a slight negative correlation (coefficient of correlation —0.329) between the amplitude obtained after 15 minutes in the dark and the light-induced fraction of the EOG

In 278 cases the amplitude of the EOG was measured on two consecutive days (24-hour interval between recordings) It was observed that in 60 per cent of these cases the change in the amplitude (increase or decrease) was less than 10 per cent and in most cases (more than 90 per cent) it was less than 20 per cent

In 19 subjects (37 periods of measurements each of four days duration) it was calculated that in 10 per cent of cases the difference between the largest and the smallest amplitude was less than 10 per cent, and in about 60 per cent of cases it was less than 20 per cent. Only in a very few cases was there a difference of as much as 50 per cent between the largest

and the smallest amplitude obtained within three consecutive 24 hour periods

Measurements repeated at monthly intervals showed (25 subjects 340 measurements) that in this case this difference was greater than 20 per cent in all test subjects and in about 90 per cent of cases the difference was less than 50 per cent of the smallest amplitude Only in nine test subjects could measurements made at monthly intervals be extended over a period of ten months In this series of measurements the difference between the smallest and largest amplitude was likewise greater than 20 per cent in all test subjects whereas in 80 per cent of cases the difference was less than 50 per cent and in all cases less than 70 per cent of the smallest amplitude.

The fact that light and darkness alter the amplitude of the corneo-fundal potential indicates the necessity of measuring the illumination in the ENG laboratory It is also necessary to make frequent calibrations of the amplitude by asking the subject to perform horizontal eye movements through a constant angle. Similar calibrations can be used to measure the slow spontaneous alterations in the amplitude. On the other hand light induced amplification of the potential can be used to improve the signal-to-noise ratio of the recordings This may facilitate the detection of nystagmus of limited amplitude

Acknowledgements

I am grateful to my teacher in oto-laryngology Professor Otto H. Meurman, M.D for his continuing interest in the progress of this investigation and for placing at my disposal all facilities of the ENG laboratory

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SUPPLEMENTUM [illegible]

ADENOIDS

Their effect on mode of breathing and nasal airflow and their relationship to characteristics of the facial skeleton and the dentition

BY

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Their effect on mode of breathing and nasal airflow and their relationship to characteristics of the facial skeleton and the dentition

A biometric rhino-manometric and cephalometro-radiographic study on children with and without adenoids

BY

STEN LINDER ARONSON

Errata

Linder Aronson, Sten Acta Oto-laryngologica, Suppl. 265

p. 18, column 2 line 8 read frontonasal for frontonasa

p. 55. table 14 line 17 read Enlarged adenoids for Enlarged adenoid

p 106, table 46, line 3 read level for leve l

p 126, column 2, line 34 read of for or

p 1?7 column ?, line 33 read awarded for a warded

p 1?9 column 1 line 8 read $n - 1$ for $n = 1$

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CONTENTS

CHAPTER 1

Review of the literature

The various opinions encountered in the literature as to a possible relationship between adenoids on the one hand and on the other special facial expressions, types of dentition and mouth breathing can be grouped as follows

1 The combination of adenoids and mouth breathing gives rise to a special facial expression and type of dentition

2 The combination of adenoids and mouth breathing does not affect the facial expression and type of dentition

3 Adenoids lead to mouth breathing in cases with particular facial characteristics and types of dentition

1 The combination of adenoids and mouth breathing gives rise to a special facial expression and type of dentition

The blocking of the nasopharynx by adenoids with the diminution or cessation of nasal breathing has been presented as a mechanism to explain the alteration of normal growth and development of the jaws The assumption is that the absence of nasal breathing may indirectly affect the form of the maxillary arch through interference with the growth of the upper facial skeleton as a whole and with the floor of the nasal cavities in particular

Once attention had been drawn by Meyer (1868) to the deleterious effect of adenoids on the hearing as well as on the general condition of a growing child, only a few years passed before Tomes (1872) reported that children who are mouth breathers on account of large adenoids usually display contracted, V shaped dental arches This form of jaw has been attributed to the circumstance that mouth breathers keep the lips parted and the tongue low the theory being that imbalance between pressure from the tongue and the cheek muscles results in the alveolar process in the premolar region being pressed medially by the cheek muscles at the same time as the anterior part of the upper jaw is pressed forwards. This line of reasoning has been termed the *compression theory* (Nordlund 1918) Many other authors, e g. Anele (1907) Körbitz (1910) Izard (1925), Bowen & Balyeat (1934) Neivert (1939) Cooke (1940) McCoy (1941) Hemley (1944) Massler Poncher & Schour (1945) Subtelny (1954) Negus (1955) Duyzing (1963) and Moyers (1963) appear to be of much the same opinion when they maintain that the direct cause of the deformation of the alveolar process in mouth breathers, partly as a consequence of adenoids, lies in the atypical movements of the tongue or other facial muscles that are usually associated with mouth breathing

Körner (1891) and Bentzen (1903) have suggested that mouth breathing in association with adenoids, besides leading to narrow dental arches may also give rise to compression of the upper jaw According to this view the height of the palatal vault increases to the same extent as the nasal cavity becomes atrophied as a result of inactivity This has been termed the *inactivity theory* (Nordlund, 1918)

Bloch (1903) and Michel (1908) believed that the high palate which develops when there is an impediment to nasal breathing is a result of the upward direction of the air stream which impinges on the palate in mouth breathing. This has been termed the *excavation theory* (Nordlund 1918)

Kantorowicz (1916) and Wustrow (1917) have expressed the view that the high palate

in cases with mouth breathing and nasal obstruction is due to the raised negative air pressure in the nasal cavity and the resulting increased difference between the pressure in the mouth and nasal cavity

Joshi (1964) found in 387 children that oronasal breathers, in association with enlarged tonsils and adenoids, are far more likely to develop Angle class II. 1 than nasal breathers.

Ricketts (1968) reporting that adenoid children displayed definite characteristics in facial expression and type of dentition, termed these observations "the respiratory obstruction syndrome Characteristic findings in these children, who are mouth breathers, are considered to be protrusion of the tongue between the upper and lower incisors in swallowing, the occurrence of open bite, uni- or bi-lateral crossbite and the head tilted backwards somewhat. Furthermore unilateral crossbite is reported to have corrected spontaneously in three patients after adenoidectomy

2. The combination of adenoids and mouth breathing does not affect the facial expression and type of dentition

Several authors have reported that so-called adenoid facies is not always associated with adenoids and mouth breathing, and that a particular type of dentition is not always found in mouth breathers with or without adenoids.

As early as 1888 Kingsley stated that he could not accept the view that muscular contraction of the cheeks could produce a contraction of the palate He felt that the V-shaped palate was inherited and not acquired through mouth breathing.

In connection with extensive facial measurements, Siebenmann (1897) found that adenoids commonly occur in leptoprosopic individuals but were not therefore etiologically responsible for this form of face

McKenzie (1909) investigated 222 children with adenoids and found that over 40% had normal palates and that deformed palates occurred in children who never had adenoids.

In a study of 800 children who underwent adenoidectomy or tonsillectomy Whitaker (1911) found that only about 30% had had dental anomalies that called for orthodontic treatment. Whitaker has also suggested that maxillary contraction with irregular dentition and the presence of adenoids and hypertrophic tonsils are both a consequence of thyroid hormone deficiency Besides leading to impaired calcification of the jaws, this deficiency activates the organism's defense mechanisms, including hypertrophy of lymphoid tissue Whitaker has pointed out, moreover that the simultaneous occurrence of mouth breathing and some form of malocclusion does not necessarily indicate a causal connection.

Nordlund (1918) investigated 61 individuals with adenoids and found that their upper jaw was characterized by a high, narrow palate This was interpreted as a consequence of a leptoprosopic inheritance

Nor could Wallace (1927) find sufficient evidence that the occurrence of adenoids leads to a particular type of dentition.

Brash (1929) like McKenzie, found that a small high palate occurred frequently among children who had never been troubled by adenoids.

Howard (1932) studied the status of the dentition of 159 children who were mouth breathers as a result of adenoids or enlarged tonsils. Only 13 9% belonged to Angle class II 1 i e the dentition often associated with mouth breathing in the literature, while 80 4% had a normal dentition and 5 7% belonged to Angle class III

Sillman (1942) conducted a longitudinal study on children from birth to 5 years of age and did not find that adenoids and mouth breathing constitute a primary etiological factor in malocclusions.

In a review of the literature on mouth breathing as a cause of special types of dentition, Hartsook (1946) concluded that mouth breathing is not a primary etiological factor in any type of malocclusion.

Since various types of dentition are found

Review of the literature

The various opinions encountered in the literature as to a possible relationship between adenoids on the one hand and on the other special facial expressions types of dentition and mouth breathing can be grouped as follows.

1 The combination of adenoids and mouth breathing gives rise to a special facial expression and type of dentition

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1 The combination of adenoids and mouth breathing gives rise to a special facial expression and type of dentition

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Joshi (1964) found in 387 children that oronasal breathers, in association with enlarged tonsils and adenoids, are far more likely to develop Angle class II. 1 than nasal breathers

Ricketts (1968) reporting that adenoid children displayed definite characteristics in facial expression and type of dentition, termed these observations "the respiratory obstruction syndrome Characteristic findings in these children, who are mouth breathers are considered to be protrusion of the tongue between the upper and lower incisors in swallowing, the occurrence of open bite uni- or bi-lateral crossbite and the head tilted backwards somewhat. Furthermore, unilateral crossbite is reported to have corrected spontaneously in three patients after adenoidectomy

2 The combination of adenoids and mouth breathing does not affect the facial expression and type of dentition

Several authors have reported that so-called adenoid facies is not always associated with adenoids and mouth breathing, and that a particular type of dentition is not always found in mouth breathers with or without adenoids.

As early as 1888 Kingsley stated that he could not accept the view that muscular contraction of the cheeks could produce a contraction of the palate He felt that the V-shaped palate was inherited and not acquired through mouth breathing.

In connection with extensive facial measurements, Siebenmann (1897) found that adenoids commonly occur in leptoprosopic individuals but were not therefore etiologically responsible for this form of face

McKenzie (1909) investigated 2__ children with adenoids and found that over 40% had normal palates and that deformed palates occurred in children who never had adenoids.

In a study of 800 children who underwent adenoidectomy or tonsillectomy Whitaker (1911) found that only about 30% had had dental anomalies that called for orthodontic treatment. Whitaker has also suggested that maxillary contraction with irregular dentition and the presence of adenoids and hypertrophic tonsils are both a consequence of thyroid hormone deficiency Besides leading to impaired calcification of the jaws, this deficiency activates the organism s defense mechanisms including hypertrophy of lymphoid tissue Whitaker has pointed out, moreover that the simultaneous occurrence of mouth breathing and some form of malocclusion does not necessarily indicate a causal connection.

Nordlund (1918) investigated 61 individuals with adenoids and found that their upper jaw was characterized by a high, narrow palate. This was interpreted as a consequence of a leptoprosopic inheritance

Nor could Wallace (1927) find sufficient evidence that the occurrence of adenoids leads to a particular type of dentition.

Brash (1929), like McKenzie, found that a small high palate occurred frequently among children who had never been troubled by adenoids.

Howard (193_) studied the status of the dentition *of 159* children who were mouth breathers as a result of adenoids or enlarged tonsils *Only 13.9%* belonged to Angle class II 1 *i.e.* the dentition often associated with mouth breathing in the literature, while 80 4% had a normal dentition and 5 7% belonged to Angle class III

Sillman (1942) conducted a longitudinal study on children from birth to 5 years of age and did not find that adenoids and mouth breathing constitute a primary etiological factor in malocclusions

In a review of the literature on *mouth* breathing as a cause of special types of dentition, Hartsook (1946) concluded that mouth breathing is not a primary etiological factor in any type of malocclusion.

Since various types of dentition are found

Review of the literature

The *various opinions* encountered in the literature as to a possible relationship between adenoids on the one hand and, on the other special facial expressions, types of dentition and mouth breathing can be grouped as follows

1 The combination of adenoids and mouth breathing gives rise to a special facial expression and type of dentition

2 The combination of adenoids and mouth breathing does not affect the facial expression and type of dentition

3 Adenoids lead to mouth breathing in cases with particular facial characteristics and types of dentition

1 The combination of adenoids and mouth breathing gives rise to a special facial expression and type of dentition

The blocking of the nasopharynx by adenoids with the diminution or cessation of nasal breathing has been presented as a mechanism to explain the alteration of normal growth and development of the jaws The assumption is that the absence of nasal breathing may indirectly affect the form of the maxillary arch through interference with the growth of the upper facial skeleton as a whole and with the floor of the nasal cavities in particular

Once attention had been drawn by Meyer (1868) to the deleterious effect of adenoids on the hearing as well as on the general condition of a *growing child only a few years passed* before Tomes (1872) reported that children who are mouth breathers on account of large adenoids usually display contracted, V-shaped dental arches This form of jaw has been attributed to the circumstance that mouth breathers keep the lips parted and the tongue low the theory being that imbalance between pressure from the tongue and the cheek muscles results in the alveolar process in the premolar region being pressed medially by the cheek muscles at the same time as the anterior part of the *upper jaw is pressed forwards. This line* of reasoning has been termed the *compression theory* (Nordlund *1918*) Many other authors, e g. Angle (1907) Körbitz (1910) Izard (1925) Bowen & Balyeat (1934) Neivert (1939) Cooke (1940) McCoy (1941) Hemley (1944) Massler Poncher & Schour (1945) Subtelny (1954) Negus (1955) Duyzing (1963) and Moyers (1963) appear to be of much the same opinion when they maintain that the direct cause of the deformation of the alveolar process in mouth breathers, partly as a consequence of adenoids lies in the atypical movements of the tongue or other facial muscles that are usually associated with mouth breathing

Körner (1891) and Bentzen (1903) have suggested that mouth breathing in association with adenoids besides leading to narrow dental arches, may *also give rise to compression of* the upper jaw According to this view the height of the palatal vault increases to the same extent as the nasal cavity becomes atrophied as a result of inactivity This has been termed the *inactivity theory* (Nordlund, 1918)

Bloch (1903) and Michel (1908) believed that the high palate which develops when there is an impediment to nasal breathing, is a result of the upward direction of the air stream, which impinges on the palate in mouth breathing. *This has been termed the excavation theory* (Nordlund 1918)

Kantorowicz (1916) and Wustrow (1917) have expressed the view *that the high palate*

sessed in relation to the size of the skeletal nasopharyngeal cavity

Subtelny (1954) strongly emphasized that not all adenoid children are mouth breathers. Mouth breathing is not considered to arise unless adenoids occupy the greater part of the nasopharyngeal airway It is also pointed out that most children who breathe through the mouth on account of adenoids display a spontaneous return to nose breathing as the lymphoid tissue becomes atrophic and the nasopharynx grows.

It has been pointed out by Goldman & Bachman (1958) that the size of the nasopharynx varies considerably in different individuals. This variation provides an important explanation for the varying effect which large adenoids have on the passage of air

Linbarth (1960) pointed out that children often had a small nasopharynx, so that nose breathing may b impeded by only a moderate enlargement of adenoids.

Discussion

As indicated above, the effect of adenoids on facial expression, types of dentition and mode of breathing has been investigated and discussed by a good many authors in the course of the past hundred years and divers opinions have been expressed as to the importance of adenoids for the development of the individual's face and dentition.

A review of the literature on this subject during this period gives the impression that several theories which were constructed on a weak foundation at an early stage have since been repeated on several occasions. In most of the cases in which the opinions have been based on investigations, the presentation of the material and methods leaves a good deal to be desired. In the majority of cases the investigations have simply taken the form of frequency studies.

Only a few reports indicate how the adenoids have been assessed. The possibilities of radiographic diagnosis were recognized at an early stage, however and were described by Mignon (1898) soon after the clinical value of x-rays became apparent.

Moreover there are few articles which indicate whether the various investigations were conducted in collaboration with an otologist.

Only some authors describe how they registered mouth breathing. In these cases this was done with the help of a cold mirror tissue paper or a metal spatula held alternately in front of the nose and mouth

Judging from the available literature, therefore, the relationship between adenoids on the one hand and adenoid facies, special types of dentition and mouth breathing on the other has so far been studied objectively to only a limited extent. In those cases in which measurements have been made, the analysis has been confined to simple methods for calculating means and percentages.

among mouth breathers, it cannot be said that there is one particular or classic type of mal occlusion

Similar opinions were expressed by Huber & Reynolds (1946) after a study on 27 mouth-breathing students, of whom one had an anatomically correct dentition, 15 Angle class I 8 Angle class II and 2 Angle class III.

In studies covering more than 15 years, Ballard & Gwynne Evans (1958) investigated the relationship between jaw form, soft tissue morphology and mode of breathing Their results suggest that oral and facial morphology remains strikingly constant during growth Consequently they consider that mouth breathing does not cause jaw deformities and malocclusions and nor does it therefore lead to so-called adenoid facies They believe that individuals displaying the syndrome of adenoid facies, contracted maxilla narrow nasal airways and malocclusions belong to a particular morphological type They usually have a long face, high gonion angle, a narrow U- or V shaped upper dental arch and a high palate. The narrow upper jaw results in narrow nasal passages and consequently nasal breathing is more likely to be impeded in infections involving swollen nasal mucosa

In an investigation on 500 patients at an ear nose and throat department, Leech (1958) reported that a postnormal occlusion was somewhat more common than other types of dentition among the patients with adenoids. A particularly interesting finding was that Angle class II 2 occurred more frequently than Angle class II 1 although the difference was not statistically significant. The study also showed that only 10% of the adenoid individuals had a narrow upper jaw Mouth breathing was found in only 19% of these children

In a study of 297 patients Linder Aronson & Bäckström (1960) found that adenoids occurred in connection with high as well as low index values for the relationship between face breadth and height as well as between palatal breadth and height.

Tulley (1966) reported that the work of the Upper Respiratory Research Unit at Guy's Hospital, London, has shown that clinical types, who may or may not have any upper respiratory defects, e g. obstructive pad of adenoids, can be recognized from the so-called adenoid facies This is an inherited facies.

3 *Adenoids lead to mouth breathing in cases with particular facial characteristics and types of dentition*

The effect of adenoids on the mode of breathing is considered by several authors to vary according to the type of face and dentition. The nasopharyngeal volume has been considered particularly important in this context.

After extensive facial and palatal measurements, Siebenmann (1897) maintained that a high palate is commonly found in individuals with a narrow face and constricted nasal cavities In individuals with a narrow nose and small nasopharyngeal volume, adenoids often cause mouth breathing.

Nordlund (1918) studied 61 patients and found that discomfort from adenoids, e.g in the form of mouth breathing, is more pronounced among individuals with a high narrow palate and narrow nose than among those with a broad palate and nasal structure

The importance of the nasopharyngeal volume has been emphasized by Bernfeld (1927) in cases of adenoids with nasal obstruction

Brash (1929) suggested that discomfort from adenoids may be a simple indication of insufficient space in the nasopharyngeal region.

Schüller (1929) simply stated that epipharyngeal tumours, among which he included adenoids cause a greater obstruction if the epipharyngeal cavity is small and narrow

Emslie Massler & Zwemer (1952) noted that in children with a narrow nasopharyngeal passage even physiological enlargement of lymphoid tissue in the nasopharyngeal region may act as an obstruction and lead to mouth breathing

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Material and methods

MATERIAL

The present investigation was conducted on 162 children from the county of Örebro in Central Sweden. Of these children, 81 were patients and 81 served as controls.

The *patients* were all children born in the years 1955–61 who attended the Otorhinolaryngologic Department of Örebro Regional Hospital in the period 1 October 1966–30 September 1967 and were judged to present indications for adenoidectomy. This assessment was made by one of the six otologists at the Department. The distribution by year of birth and sex for all adenoidectomy cases during this period is shown in Fig. 1. The majority of the children presenting indications for adenoidectomy were about 8 years old. The sex ratio is 60% boys and 40% girls. This ratio has been compared with the sex distribution for the children who underwent adenoidectomy during 1967 at the Regional and University Hospital in Linköping (56% boys and 44% girls). The sex difference is not significant.

During the period in question, a total of 166 patients born in the years 1955–61 underwent adenoidectomy at Örebro Regional Hospital, representing 0.9% of the population. The 81 patients who form the subjects of the present investigation constitute 0.4% of the population. The difference between the total number of adenoidectomy patients and the present group of subjects amounts to 85 patients. This drop-out is explained as follows:

( ) The 35 patients belonging to the Lindesberg district were not included for practical reasons.

(*b*) The 13 patients who underwent adenoidectomy at the regional hospital but whose treatment was otherwise in the hands of private specialists were not included either.

(*c*) Adenoidectomy was performed on 30 patients at the regional hospital without the Orthodontic Department at Örebro being informed.

(*d*) Adenoidectomy was performed on 7 patients at the regional hospital at times when data could not be registered at the Orthodontic Department before the operation.

The *control group* was made up to conform to the age, sex and number of the adenoidectomy children. Thus the controls were selected by taking the child resident in Örebro whose national registration number came closest after that of one of the adenoidectomy children of the same sex. This means that the controls were of practically the same age as the patients. The controls were confined to residents of Örebro in order to make it easier for these children to participate in the investigation.

Further selection criteria for the controls were that they had no history of obstructed nose breathing, allergy or recurrent otitis media and infections that they had never undergone adenoidectomy or received orthodontic treat

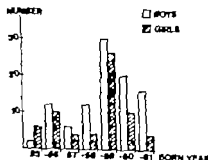


Fig. 1. Distribution of the total material by sex and year of birth. The investigation was made in the period 1 October 1966–30 September 1967

CHAPTER 2

Aim of the present investigation

In view of the divergency of opinions concerning the relationship of adenoids to mode of breathing and special types of facial expression and dentition—and consequently also the uncertainty *as to whether adenoidectomy can be* expected to influence the status of the dentition—the present investigation was conducted with the primary aim of using objective methods of registration together with correlation analysis and multiple regression analysis to study what effect the presence of adenoids has on variables that represent airflow mode of breathing and type of dentition

At the same time an attempt is made to study the relationship between these variables and certain variables for the facial skeleton

The investigation also includes an analysis of the possibility of a connection between adenoids and so-called adenoid facies

The question of whether changes in tongue position are of etiological importance for mal occlusions in the presence of adenoids is approached by studying the correlations between *variables for tongue position and variables for* size of adenoids and dentition In this context particular attention is paid to the variables for arch width arch length height of palatal vault, and inclination of upper and lower incisors

The relationship between size of adenoids and the values for the dentition variables was studied on the basis of the following working hypothesis.

Enlarged adenoids gives rise to mouth breathing, which leads in turn to a change in tongue position and this is then followed by changes that are reflected in the dentition variables.

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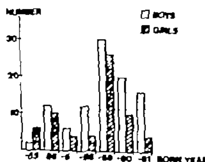


Fig. 1 Distribution of the total material by sex and year of birth. The investigation was made in the period 1 October 1966–30 September 1967

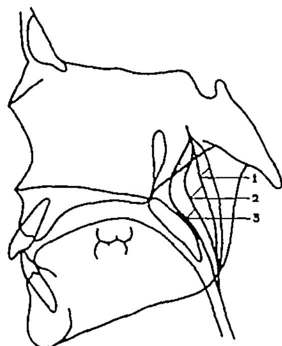


Fig 2 Grouping by size of adenoids as studied on lateral cephalometric radiographs. 1 – no adenoids, 2 – small or moderate adenoids, 3 – large adenoids.

ment and were willing to take part in the study If these criteria were not fulfilled by the child whose registration number came closest after an adenoidectomy child—as happened in five cases—then the child of the same sex with the next nearest number who met the criteria was selected inste d Of the five children who did not meet the criteria one had previously received orthodontic treatment two had previously undergone adenoidectomy and two had had such discomfort from nose breathing that an otologist had considered that adenoidectomy was indicated (these two were later included among the adenoidectomy patients)

The control group which comprises children from the city of Örebro represents about 1 % of the population of Örebro city born in the years 1955–61

The controls were examined at the Otorhinolaryngologic Department either by the Head or the Deputy Head Otologist

Grouping

The controls were grouped according to the size of the adenoids as assessed on lateral radiographs (cf Fig. 2)

Group 1 No adenoids 37 children.

Group 2. Small or moderate adenoids. 33 children

Group 3 Large adenoids. 11 children.

The adenoidectomy patients were grouped according to the indication for the operation

Group 4 Adenoidectomy as a result of recurrent otitis media. 21 children.

Group 5 Adenoidectomy as a result of obstructed nose breathing: 60 children

Patients with both these indications were referred to group 5

The selection of patients for groups 4 and 5 was undertaken by the otologists and is thus based upon clinical observations as to the presence of adenoids as well as the presence of ear nose and throat complaints in the form of recurrent otitis media and obstructed nose breathing. The controls, on the other hand, were grouped solely according to the size of the adenoids as assessed by the author from lateral radiographs.

Variables

In order to make the investigation as comprehensive as possible 173 variables were chosen preliminarily as being possibly relevant and were studied in all the patients in the material. Statistical processing of the results showed however that the number of variables could be reduced to 131 The variables excluded are those which correlation analysis proved to be irrelevant in the present context particularly in relation to the airflow mode of breathing and dentition variables The majority of those excluded were index variables

The final list of 131 variables, which is presented and defined in Table I and on pages 13–15 can be divided into the following groups

Group An 19 variables concerning the anamnesis and clinical status This group comprises all the anamnestic and status data noted by the otologists and/or the author at the first examination

Group Ad. 22 adenoid variables This group covers the various indications for adenoidec

Table 1 *The variables and their definitions*

The variables are arranged in seven groups. *An*, anamnesis and clinical variables, *Ad*, adenoid variables; *D* dentition variables; *F* airflow variables; *G* variable for grouping the children, *S*, skeleton and lip variables; *T* variables for tongue position

Variable no.	Variable	Unit etc.	Definition on page
	Group An, Anamnesis and clinical status		
	Anamnestic data.		
A01	Number		
A02	Age	Year of birth	
A03	Sex	Boy 0, girl 1	
A04	Mode of breathing	Nose 0, mouth 1 both 2	
A05	Mouth in sleep	Closed 0, open 1	
A06	Infections in ear, nose & throat	No 0, yes 1	
A07	Allergy	No 0, yes 1	
A08	Previous adenoidectomy	No 0, yes 1	
A09	Siblings with ear nose & throat diseases	No 0, yes 1	
A10	Prolonged finger-sucker	No 0, yes 1	
A11	Previous orthodontic therapy	No 0, yes 1	
	Clinical assessments.		
A12	Open or closed mouth	Closed 0, open 1	
A13	Obstructed nose breathing, left	No 0, yes 1	
A14	Obstructed nose breathing, right	No 0, yes 1	
A15	Mouth breathing	No 0, yes 1	
A16	Enlarged adenoids	No 0, yes 1	
A17	Large tonsils	No 0, yes 1	
A18	Swollen nasal mucosa	No 0, yes 1	
A19	Septum deviation	No 0, yes 1	
	Group Ad, Adenoid variables		
A20	Adenoid size before adenoidectomy	Radiogr assessment, no adenoids 1 small 2, moderate 3 large 4 very large 5	
A21	Adenoid size after adenoidectomy		
	Indication for adenoidectomy		
A22	Obstructed nose breathing	No 0, yes 1	
A23	Recurrent infection	No 0, yes 1	
A24	Recurrent otitis media	No 0, yes 1	
A25	Allergy	No 0, yes 1	
	Adenoid size measured on cephalom. radiogr		
A26	ad_1–ba preop.	mm	
A27	ad_1–ba postop.	mm	20
A28	ad_1–ba difference	mm	
A29	ad_2–ho preop.	mm	
A30	ad_2–ho postop	mm	20
A31	ad_2–ho difference	mm	
A32	$\frac{\text{Adenoid area} \cdot 100}{\text{pm–ho–ba–pm}}$ preop		
A33	$\frac{\text{Adenoid area} \cdot 100}{\text{pm–ho–ba–pm}}$ postop.		22
A34	$\frac{\text{Adenoid area} \cdot 100}{\text{pm–ho–ba–pm}}$ difference		
A35	$\frac{\text{Adenoid area} \cdot 100}{\text{pm–ho–ba–ho'–pm}}$ preop.	%	
A36	$\frac{\text{Adenoid area} \cdot 100}{\text{pm–ho–ba–ho'–pm}}$ postop.		22
A37	$\frac{\text{Adenoid area} \cdot 100}{\text{pm–ho–ba–ho'–pm}}$ difference		
A38	$\frac{ad_2\text{–ho} \cdot 100}{\text{pm–ho}}$ preop		
A39	$\frac{ad_2\text{–ho} \cdot 100}{\text{pm–ho}}$ postop.		22

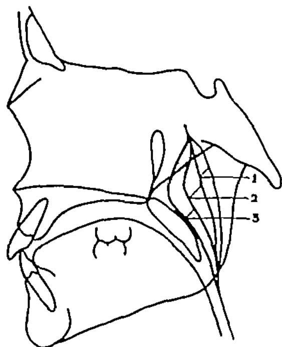


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Group An 19 variables concerning the anamnesis and clinical status This group comprises all the anamnestic and status data noted by the otologists and/or the author at the first examination

Group Ad 22 adenoid variables. This group covers the various indications for adenoidec

Table 1 *The variables and their definitions*

The variables are arranged in seven groups. *An*, anamnesis and clinical variables, *Ad*, adenoid variables; *D* dentition variables; *F* airflow variables; *G* variable for grouping the children; *S*, skeleton and lip variables; *T* variables for tongue position

Variable no.	Variable	Unit etc.	Definition on page
	Group An, Anamnesis and clinical status		
	Anamnestic data.		
A01	Number		
A02	Age	Year of birth	
A03	Sex	Boy 0, girl 1	
A04	Mode of breathing	Nose 0, mouth 1 both 2	
A05	Mouth in sleep	Closed 0, open 1	
A06	Infections in ear nose & throat	No 0, yes 1	
A07	Allergy	No 0, yes 1	
A08	Previous adenoidectomy	No 0, yes 1	
A09	Siblings with ear nose & throat diseases	No 0, yes 1	
A10	Prolonged finger-sucker	No 0, yes 1	
A11	Previous orthodontic therapy	No 0, yes 1	
	Clinical assessments:		
A12	Open or closed mouth	Closed 0, open 1	
A13	Obstructed nose breathing, left	No 0, yes 1	
A14	Obstructed nose breathing, right	No 0, yes 1	
A15	Mouth breathing	No 0, yes 1	
A16	Enlarged adenoids	No 0, yes 1	
A17	Large tonsils	No 0, yes 1	
A18	Swollen nasal mucosa	No 0, yes 1	
A19	Septum deviation	No 0, yes 1	
	Group Ad, Adenoid variables		
A20	Adenoid size before adenoidectomy	Radiogr assessment no adenoids 1 small 2, moderate 3, large 4, very large 5	
A21	Adenoid size after adenoidectomy		
	Indication for adenoidectomy:		
A22	Obstructed nose breathing	No 0 yes 1	
A23	Recurrent infection	No 0, yes 1	
A24	Recurrent otitis media	No 0, yes 1	
A25	Allergy	No 0, yes 1	
	Adenoid size measured on cephalom. radiogr		
A26	ad_1–ba preop.	mm	
A27	ad_1–ba postop.	mm	20
A28	ad_1–ba difference	mm	
A29	ad_2–ho preop.	mm	
A30	ad_2–ho postop.	mm	20
A31	ad_2–ho difference	mm	
A32	$\frac{\text{Adenoid area}\ 100}{\text{pm–ho–ba–pm}}$ preop	%	22
A33	$\frac{\text{Adenoid area}\ 100}{\text{pm–ho–ba–pm}}$ postop.	%	
A34	$\frac{\text{Adenoid area}\ 100}{\text{pm–ho–ba–pm}}$ difference		
A35	$\frac{\text{Adenoid area}\ 100}{\text{pm–ho–ba–ho'–pm}}$ preop.		22
A36	$\frac{\text{Adenoid area}\ 100}{\text{pm–ho–ba–ho'–pm}}$ postop	%	
A37	$\frac{\text{Adenoid area}\ 100}{\text{pm–ho–ba–ho'–pm}}$ difference	%	
A38	$\frac{ad_2\text{–ho}\ 100}{\text{pm–ho}}$ preop.		22
A39	$\frac{ad_2\text{–ho}\ 100}{\text{pm–ho}}$ postop.		

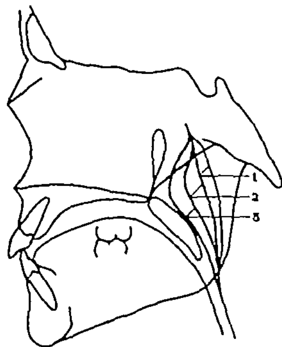


Fig 2 Grouping by size of adenoids as studied on lateral cephalometric radiographs. 1 – no adenoids, 2 – small or moderate adenoids, 3 – large adenoids.

ment and were willing to take part in the study If these criteria were not fulfilled by the child whose registration number came closest after an adenoidectomy child—as happened in five cases—then the child of the same sex with the next nearest number who met the criteria was selected inste d Of the five children who did not meet the criteria, one had previously received orthodontic treatment, two had pre viously undergone adenoidectomy and two had had such discomfort from nose breathing that an otologist had considered that adenoidectomy was indicated (these two were later included among the adenoidectomy patients)

The control group which comprises children from the city of Örebro represents about 1% of the population of Örebro city born in the years 1955–61

The controls were examined at the Otorhinolaryngologic Department either by the Head or the Deputy Head Otologist

Grouping

The controls were grouped according to the size of the adenoids as assessed on lateral radiographs (cf Fig. 2)

Group 1 No adenoids 37 children.

Group 2. Small or moderate adenoids. 33 children

Group 3 Large adenoids. 11 children

The adenoidectomy patients were grouped according to the indication for the operation

Group 4 Adenoidectomy as a result of recurrent otitis media. 21 children.

Group 5 Adenoidectomy as a result of obstructed nose breathing 60 children.

Patients with both these indications were referred to group 5

The selection of patients for groups 4 and 5 was undertaken by the otologists and is thus based upon clinical observations as to the presence of adenoids as well as the presence of ear nose and throat complaints in the form of recurrent otitis media and obstructed nose breathing. The controls, on the other hand, were grouped solely according to the size of the adenoids as assessed by the author from lateral radiographs

Variables

In order to make the investigation as comprehensive as possible 173 variables were chosen preliminarily as being possibly relevant and were studied in all the patients in the material. Statistical processing of the results showed, however that the number of variables could be reduced to 131 The variables excluded are those which correlation analysis proved to be irrelevant in the present context particularly in relation to the airflow mode of breathing and dentition variables. The majority of those ex cluded were index variables

The final list of 131 variables which is presented and defined in Table 1 and on pages 13–15 can be divided into the following groups

Group An 19 variables concerning the anamnesis and clinical status This group com prises all the anamnestic and status data noted by the otologists and/or the author at the first examination

Group Ad 22 adenoid variables This group covers the various indications for adenoidec

Table I *Cont*

Variable no.	Variable	Unit etc.	Definition on page
A84	Height of upper lip	mm (clinical measure)	16
A85	n–s	mm	20
A86	s–ba	mm	20
A87	n–ba	mm	20
A88	n–gn	mm	20
A89	n–sp	mm	20
A90	sp–gn	mm	20
A91	ss'–pm	mm	20
A92	pm–ba	mm	20
A93	ho ⊥ pm–ba	mm	20
A94	s–pm	mm	20
A95	⊥ pm–ba	mm	20
A96	Height of upper lip	mm	21
A97	Height of lower lip	mm	21
A98	fmt–fmt	mm	19
A99	lo–lo	mm	19
A100	bch–bch	mm	19
A101	bch–bch ho ⊥ pm–ba pm–ba ½	cu. mm	
A102	s–n–ss	degrees	21
A103	s–n–sm	degrees	21
A104	s–n–ss 82°	No 0, yes 1	
A105	ss–n–sm	degrees	21
A106	ML/NSL	degrees	21
A107	ML/NL	degrees	21
A108	NL/NSL	degrees	21
A109	ba–s–pm	degrees	21
A110	n–s–ba	degrees	21
A111	Face width 100 / Face height	– (clinical measure) A80/A81	16
A112	fmt–fmt 100 / n–gn	–	21
A113	lo–lo 100 / n–gn		21
A114	n–s 100 / n–gn	–	21
A115	ss–pm 100 / n–gn		21
A116	n–sp 100 / n–gn	%	21
A117	ss' pm 100 / n–sp		22
A118	ho–ba 100 / pm–ba	%	22
A119	s–ba 100 / n–s		22
A120	pm–ba 100 / ho ⊥ pm–ba	%	22
A121	pm–ho	mm	20
A122	ba–ho	mm	20
A123	ho ⊥ pm–ba pm–ba ½	sq. mm	
A124	ss–n–ba	degrees	21
A125	pm–ho–ba	degrees	21
A126	n–ho	mm	20
A127	s–ho	mm	20
A128	Body height	cm	
	Group T Variables for tongue position		
A129	pm–t_1 preop rest position	mm	20
A130	ba–t_4 preop rest position	mm	20
A131	$\frac{pm–v}{2}$ t_4 preop. rest position	mm	20

Table 1 *Cont*

Variable no.	Variable	Unit etc.	Definition on page
A40	$\frac{ad_1\text{–}ba \times 100}{pm\text{–}ba}$ preop.	%	22
A41	$\frac{ad_1\text{–}ba \quad 100}{pm\text{–}ba}$ postop	%	
	Group D Dentition variables		
A42	ss & sm projected on OL	mm	20
A43	Freeway space preop.	mm	18
A44	OL/ML	degrees	21
A45	OL/NSL	degrees	21
A46	IL_s/NSL (measure of retroclination)	degrees	21
A47	IL_s/IL_i	degrees	21
A48	IL_i/ML (measure of retroclination)	degrees	21
A49	Arch width M_1–M upper	mm	22
A50	Arch width M_1–M lower	mm	22
A51	Arch width 04–04 upper	mm	22
A52	Arch width 04–04 lower	mm	22
A53	Arch length upper	mm	3
A54	Arch length lower	mm	23
A55	Overjet	mm	23
A56	Overbite	mm	23
A57	Sagittal relation M M right	mm	24
A58	Sagittal relation M M left	mm	4
A59	Crossbite	No 0 yes 1	22
A60	Height of palatal vault at M –M	mm	23
A61	Space difference of upper arch	mm	23
A62	Space difference of lower arch	mm	23
A63	$\frac{\text{Lower arch width } M_1\text{–}M \quad 100}{\text{Upper arch width } M_1\text{–}M}$	%	24
A64	$\frac{\text{Lower arch width 04–04} \quad 100}{\text{Upper arch width 04–04}}$		24
A65	$\frac{\text{Upper arch length} \quad 100}{\text{Upper arch width M –M}}$		24
A66	$\frac{\text{Height of palatal vault} \quad 100}{\text{Upper arch width M –M}}$	%	4
	Group F Airflow variables	lit/min at differential pressure (mm H O) of	
A67	Preop. airflow before nose drops	10 initial value for controls	
A68	Preop airflow before nose drops	15 initial value for controls	
A69	Preop airflow before nose drops	20 initial value for controls	
A70	Preop airflow after nose drops	10 initial value for controls	
A71	Preop airflow after nose drops	15 initial value for controls	
A72	Preop airflow after nose drops	20 initial value for controls	
A73	Postop airflow before nose drops	10 value one month later for controls	
A74	Postop. airflow before nose drops	15 value one month later for controls	
A75	Postop airflow before nose drops	20 value one month later for controls	
A76	Postop airflow after nose drops	10 value one month later for controls	
A77	Postop. airflow after nose drops	15 value one month later for controls	
A78	Postop airflow after nose drops	20 value one month later for control	
	Group G Variable for grouping children		
A79	Group	*Controls* (radiogr assessment) no adenoids 1 small or mod. ad. 2, large ad. 3 Subjects (ind. for adenoidectomy) recurrent otitis media 4 nasal obstruction 5	
	Group S Skeleton and lip variables		
A80	Face width	mm (clinical measure)	16
A81	Face height	mm (clinical measure)	16
A82	Nose width over alae nasii	mm (clinical measure)	
A83	Nose width above alae nasii	mm (clinical measure)	



Fig. 4. Cephalostat according to Thörne modified for exact measurement of the angle between the Frankfort plane and the horizontal plane on postero-anterior cephalometric radiographs.

called adenoid facies (cf. Fig. 3 for a description see p. 5) varied between the patient and control groups. The occurrence of adenoid facies was assessed independently by an otologist and an orthodontist.

Measurements on the radiographs

The following radiographs were taken in each child: two lateral cephalometric radiographs with the teeth occluded, two with the lower jaw in the rest position and two postero-anterior radiographs with the teeth occluded. For the lateral radiographs the exposure times were 0.4 or 0.5 sec, while for the postero-anterior radiographs they were 1.0 or 1.. sec, the exposure being adapted to the age of the individual.

The radiographs were taken with a Philips Rotapractix apparatus with a film-focus distance of 165 cm and a rotating anode tube with a focus of 1.. mm. The exposures were made with 100 kV and 50 mA.

The radiographs were taken with the subject's head immobilized in a cephalostat ad modum Thörne (1951).

For the profile films the subject was seated with the left side facing the film. The head was fixed in the cephalostat with the median plane parallel to the film and 10 cm from it, and an aluminum filter wedge shaped in cross-section, was placed between the facial profile and the film to reduce the dosage in this area. The central ray passes through two rods inserted in the external ear channel. The enlargement of the median plane with this arrangement is 6.5%.

For the postero-anterior films the subject was seated with the face turned to the film. The head was fixed in the cephalostat in two different positions: (1) The head was orientated with the Frankfort plane horizontal (2) the head had been rotated in a forward direction to 26° between the Frankfort plane and the horizontal plane (see Fig. 4). The ear rods were placed 12 cm from the film. The enlargement of a plane through the ear rods is then 7.8%.

Definitions of the measurements on the radiographs

The measurements on the radiographs were made on Unitek tracing film no. 701-204 on which the reference points were marked. All

tomy as well as measurements of the size of the adenoids

Group D· 25 dentition variables, i.e all the variables that describe the individual's dentition

Group F 12 airflow variables, i e the variables that express the nasal airflow at differential pressures of 10 15 and 20 mm H_2O

Group G 1 variable for grouping the subjects under five headings 1–3 for the controls and 4–5 for the subjects of the investigation

Group S 47 skeletal and 2 lip variables

Group T 3 tongue variables. These variables indicate the position of the tongue in relation to the hard and soft palate

All these variables were studied in the patients as well as the controls in the following ways

1 Direct measurements on the child,

2. Lateral and frontal photographs of the face

3 Lateral and postero-anterior radiographs.

4 Casts of the upper and lower jaws

5 Recordings of nasal airflow before and 15 min after the administration of nose drops.

All the children were first examined on two occasions one month apart. In the case of the patients, the lateral radiography and airflow measurements were repeated at the second examination, which took place one month after adenoidectomy In the controls however only the airflow measurements were repeated.

In addition all the children have been followed up one year after the second examination In order to keep the present report within reasonable limits, however this part of the investigation will be presented separately

MEASUREMENTS

Direct measurements

Five direct measurements were made on each child represented by the following variables.

A80 Width of face between two points 15 mm lateral of the lateral angle of either eye



Fig 3 So-called adenoid facies.

A81 Height of face between the midpoint of the line joining the medial angles of either eye and the lower edge of the lower jaw

A82 Width of nose over alae nasi

A83 Width of nose above alae nasi

A84 Height of upper lip between the columella nasi and the lower edge of the upper lip in the median plane.

Variables A80–83 were measured with a modified caliper rule to an accuracy of ±0 1 mm Variable A84 was measured with a conventional caliper rule with the same accuracy

Photographs of the face

Frontal and profile photographs were taken of the face in every case from a distance of 1 m These photographs were used to investigate whether the frequency of individuals with so-

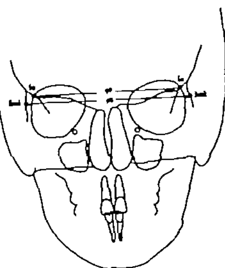


Fig 7 Reference points and linear measurements on postero-anterior cephalometric radiographs with the Frankfort plane horizontal.
fmt Frontomalare temporale—the most lateral point in the zygomaticofrontal suture (Martin 1928).
fmt–fmt Distance between fmt on either side (A98).
lo Latero-orbitale—intersection of the oblique line and the orbital margin (Samouri 1960).
lo–lo Distance between lo on either side (A99).

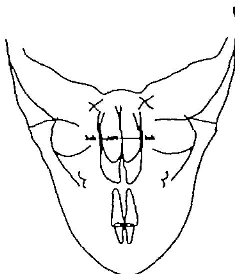


Fig 8 Reference points and linear measurements on postero-anterior cephalometric radiographs with the head rotated in forward direction so that the Frankfort plane is at 26° to the horizontal plane.
bch The most lateral point on the lateral wall of the nasal cavity
bch–bch Distance between bch on either side—width of posterior choanal aperture—(A100).

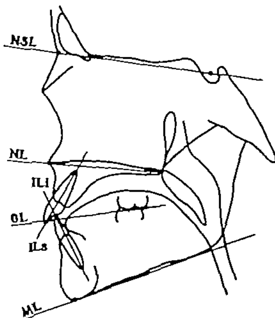


Fig 9 Reference lines on lateral cephalometric radiographs.
ILi Lower incisal line—the axis of the lower central incisor
ILs Upper incisal line—the axis of the upper central incisor
ML Mandibular line—the tangent to the lower border of the mandible through gn. (If the lower border of the mandible presented a double contour the mandibular line was taken to be line midway between the tangents to the two contours.)
NL Nasal line—the line through sp and pm.
NSL Nasion-sella line—the line through and s.
OL Occlusal line—the line through the midpoint of the distance between the incisal edges of the upper and lower central incisors and the distobuccal cusp of the first upper molar (If the first upper molar presented double contour point was chosen midway between the double contours of the apices of the distobuccal cusps.)

Indexes for skeletal variables measured on cephalometric radiographs

In addition to the measurement of lines and angles, indexes were calculated for relationships between variables for widths, heights and lengths in the face and nasopharynx. The measurements were made on cephalometric radiographs and the indexes are expressed as per centages.

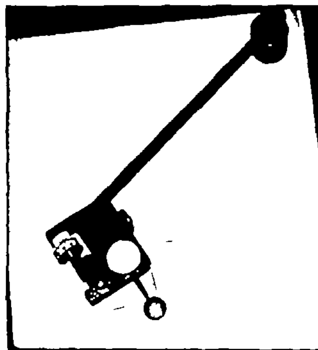
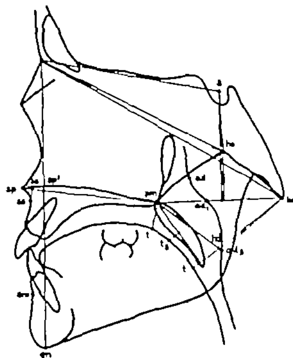


Fig 5 The Ingut 9544-11 planimeter type OTT for measuring the area of adenoids and the bony nasopharynx.



linear measurements were read to the nearest tenth of a millimetre

The angles were measured between lines defined by reference points All the readings were made to the nearest half degree

Free way space (A43) is the difference between the distance n–gn at rest and in occlusion

Area measurements of the size of adenoids and the size of the bony nasopharyngeal cavity (see p 21) were made with an Ingut 9544-11 planimeter type OTT to within ±2 sq mm (see Fig 5)

The various reference points and lines as well as the linear and angular measurements on the cephalometric radiographs are indicated in Figs 6–11 and defined in the text to these figures

Fig 6 Reference points on lateral cephalometric radiographs.

- ad Intersection of the line pm–ba and the posterior nasopharyngeal wall.
- ad Intersection of the line pm–ho and the posterior nasopharyngeal wall.
- ad_2 Intersection of the line ba–ho and the posterior nasopharyngeal wall.
- ba Basion—the most postero-inferior point on the clivus of os occipitale.
- gn Gnathion—the point on the inferior limit of the symphysis furthest from nasion.
- ho Hormion—the vomer's most dorsal contact point on the body of the sphenoid bone in the midsagittal plane, between the alae of the vomer (Martin, 1928).
- ho The point corresponding to the point ho on the opposite side of the line pm–ba.
- n Nasion—the most anterior point of the frontonasal suture.
- pm pterygomaxillare—the intersection between the nasal floor and the posterior contour of the maxilla
- s Sella—the centre of the sella turcica the upper limit of the sella turcica is defined as the line joining the tuberculum and dorsum sellae.
- s The projection of s on the line pm–ba.
- sm Supramentale—the most posterior point on the anterior contour of the lower alveolar arch (the head being oriented with the Frankfort plane parallel to the horizontal plane)
- sp Spinal point—the apex of the anterior nasal spine
- sp Intersection of the nasal line sp–pm and the line nasion–gnathion.
- ss Subspinale—the most posterior point on the anterior contour of the upper alveolar arch (the head being oriented with the Frankfort plane parallel to the horizontal plane).
- ss The projection of ss on the nasal line
- t Intersection of a line perpendicular to the nasion–sella line through pterygomaxillare and the contour of the tongue
- t Intersection of the contour of the tongue and a line through basion perpendicular to the sella basion line
- t_1 Intersection of the contour of the tongue and a line through the midpoint of and perpendicular to the line pm–v
- v The most postero-inferior point of the soft palate (tip of the uvula).

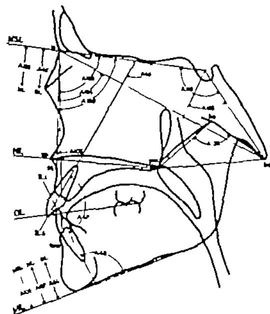


Fig 11 Angular measurements on lateral cephalometric radiographs.

s–n–ss Sella–nasion–subspinale—angle between apical base of maxilla and the line nasion–sella (A102).

s–n–sm Sella–nasion–supramentale—angle between apical base of mandible and the line nasion–sella (A103).

ss–n–sm Subspinale–nasion–supramentale—postero-anterior angle between the lines from nasion to the apical base points on the upper and lower jaws (A105).

ML/NSL Mandibular line/Nasion–sella line—relative dimension between anterior and posterior face height (A106).

ML/NL Mandibular line/Nasal line—relative dimension between anterior and posterior lower face height (A107).

NL/NSL Nasal line/Nasion–sella line—relative dimension between anterior and posterior upper face height (A108).

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dicular to the line pm–v through the midpoint of this line (A131).

Height of upper lip—the shortest distance from the contour of the upper lip to the nasal line (A96).

Height of lower lip—the shortest distance from the contour of the lower lip to the mandibular line (A97).

ad–ho–ba–ad–ad	Area of adenoids.
ad–ho–ba–ad–ad–ad	Area of adenoids.
pm–ho–ba–pm	Area of bony nasopharynx.
pm–ho–ba–ho–pm	Area of nasopharynx.

OL/ML Occlusal line/Mandibular line—relative dimension between anterior and posterior height of corpus mandibulae (A44).

OL/NSL Occlusal line/Nasion–sella line—relative dimension between anterior and posterior height of upper face plus upper section of lower face (A45).

ba–s–pm Basion–sella–pterygomaxillare—angle between the line for the posterior part of basis cranii and the line for posterior upper face height—depth of nasopharynx—(A109).

ILs/NSL Upper incisal line/Nasion–sella line—angle between the longitudinal axis of upper central incisor and the nasion–sella line (A46).

ILs/ILi Upper incisal line/Lower incisal line—incisor angle, angle between longitudinal axes of upper and lower central incisor (A47).

ILi/ML Lower incisal line/Mandibular line—angle between longitudinal axis of lower central incisor and the mandibular line (A48).

n–s–ba Nasion–sella–basion—cranial base angle, expresses curvature in midsagittal plane of the borderline between the visceral cranium and the neurocranium (A110).

ss–n–ba Subspinale–nasion–basion—angle of apical base of maxilla in relation to the line representing the length of the cranial base (A124).

pm–ho–ba Pterygomaxillare–hormion–basion—roof angle of the bony nasopharynx (A125).

Relationship between face breadth and face height:

$$\frac{\text{fmt–fmt (A98)}}{\text{n–gn (A88)}} \times 100 \qquad (A112)$$

Relationship between face breadth and face height.

$$\frac{\text{lo–lo (A99)}}{\text{n–gn (A88)}} \times 100 \qquad (A113)$$

Relationship between length of the anterior part of basis cranii and face height:

$$\frac{\text{n–s (A85)}}{\text{n–gn (A88)}} \times 100 \qquad (A114)$$

Relationship between length of basis maxillae and face height.

$$\frac{\text{ss–pm (A91)}}{\text{n–gn (A88)}} \times 100 \qquad (115)$$

Relationship between upper and total face height.

$$\frac{\text{n–sp (A89)}}{\text{n–gn (A88)}} \times 100 \qquad (A116)$$

Relationship between basis maxillae and upper face height.

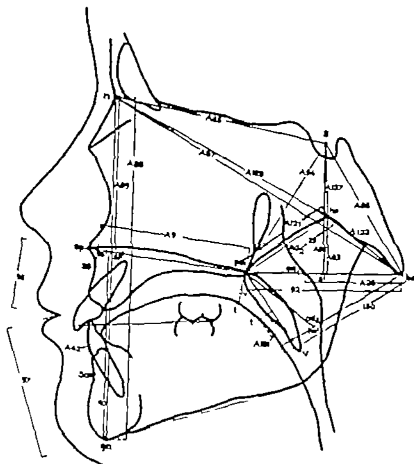


Fig 10 Linear and area measurements on lateral cephalometric radiographs.

n–s — Nasion–sella—length of anterior part of basis cranii (A85).

s–ba — Sella–basion—length of posterior part of basis cranii (A86).

n–ba — Nasion–basion—length of basis cranii (A87).

n–gn — Nasion–gnathion—anterior face height (A88).

n–sp — Nasion to the intersection of NL and the line n–gn—anterior upper face height measured along n–gn in m dsagittal plane (A89).

sp–gn — Gnathion to the intersection of NL and the line n–gn—anterior lower face height measured along n–gn in midsagittal plane (A90)

ss–pm — Subspinale projected on NL to pterygomaxillare—length of basis maxillae and an expression for the length of the floor of the nasal cavity (A91).

pm–ba — Pterygomaxillare to basion—depth of bony nasopharynx (A92).

ho ⊥ pmba — Perpendicular on pterygomaxillare-basion through hormion—height of bony nasopharynx (A93)

s–pm — Sella to pterygomaxillare—posterior upper face height (A94).

ad_1–ba — Intersection of posterior wall of the nasopharynx and the line pmba–basion—thickness f adenoids measured along pm–ba (A26).

Note that in this study the sagittal d mensions of the nasopharynx are referred to as depths and the sagittal dimensions of the maxillary body and nasal cavity are referred to as lengths.

s ⊥ pmba — Perpendicular on pterygomaxillare-basion through sella—distance between the midpoint of sella turcica and its projection on pm–ba (A95).

ss sm — Subspinale to supramentale—distance between subspinale and supramentale projected onto the occlusal l ne (A42).

ad ho — Intersection of posterior wall of the nasopharynx and the line pmho–hormion—thickness of adenoids measured along pm–ho (A29)

pm–ho — Pterygomaxillare to hormion—length of dorsal margin of vomer and an expression for the length of the pterygoid process or of the posterior choanal aperture (Bergland 1963) (A121).

ba–ho — Basion–hormion—length of the total pharyngeal clivus (Bergland 1963) (A1..).

n–ho — Nasion–hormion—length of the roof of the nasal ca ity (Bergland 1963) (A176)

s–ho — Sella hormion—approximate vertical dimension of the body of the sphenoid bone (Bergland 1963)(A127).

pm–t — Pterygomaxillare to the co tour of the t ngue—this distance measured along a perpendicular to NSL through pterygomaxillare (A179).

ba–t — Basi n to the contour of the tongue—this distance measured along perpendicular to the line s–ba thr ugh basion (A130).

pm–/s – t — Contour of soft palat to contour of the tongue—this distance measured along a perpen-

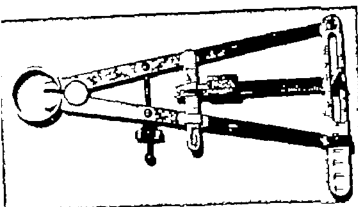


Fig 13 Three-dimensional calipers designed by Korkhaus (and modified by Lundström) for measuring the length of the dental arch and the height of the palatal vault.

was measured in the same way as in the upper jaw

A 2. *The length of the dental arch* as measured (to within ±0 1 mm) with the three-dimensional calipers (compass) designed by Korkhaus and modified by Lundström (see Fig. 13) The measurements were made in accordance with Lundström (1948)

A 3 The space-difference of the dental arch. The difference between the circumference of the dental arch from second molar to second molar and the sum of the mesiodistal diameter of first molar premolars, canines and incisors. The mesiodistal tooth diameter and the space of the dental arch were measured in accordance with Lundström (1948) (see Fig. 14)

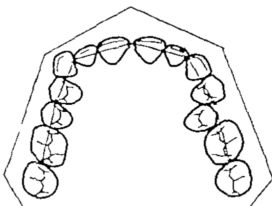


Fig 14 Measuring the space in the dental arch. After Lundström.

B 1 The height of the palatal vault, i.e. to its highest point, was measured at right angles to the plane of occlusion, in the line joining the measuring points on the first molars. The threedimensional compass was used for this measurement as well, placed in the same way as in measurement of the length of the dental arch (see Fig. 15) The measurements were made in accordance with Lundström (1948), with an accuracy of ±0 1 mm.

C 1 The overjet was measured, with an accuracy of ±0 1 mm, at the central incisors, using the sliding calipers. The overjet was taken as the mean of the distance from the midpoint of the edge of the left upper central incisor to the labial surface of the left lower central incisor and of the corresponding distance between the right upper central incisor and right lower central incisor The relevant distance was measured parallel to the plane of occlusion, at right angles to the dental arch (see Fig. 16)

C 2. The overbite was also measured at the central incisors. It is given as the mean of the distance from the edge of the left lower central incisor to the point on its labial surface on which the sliding calipers impinged in measurement of the overjet, and of the corresponding distance on the right lower central incisor A horizontal groove was drawn through this point (see Fig. 16) Using the sliding calipers, the distance was measured with an accuracy of ±0 1 mm. A frontally open bite is denoted by a negative value, and the reverse by a positive value.

C 3 The molar occlusion was taken as the

$$\frac{\text{s-pm (A91)}}{\text{n-sp (A89)}} \times 100 \qquad \text{(A117)}$$

Relationship between length of total pharyngeal clivus and depth of bony nasopharynx

$$\frac{\text{ho-ba (A122)} \times 100}{\text{pm-ba (A92)}} \qquad \text{(A118)}$$

Relationship between posterior and anterior parts of basis cranii

$$\frac{\text{s-ba (A86)}}{\text{n-s (A85)}} \times 100 \qquad \text{(A119)}$$

Relationship between depth and height of bony nasopharynx

$$\frac{\text{pm-ba (A92)}}{\text{ho} \perp \text{pm-ba (A93)}} \times 100 \qquad \text{(A120)}$$

Relationship before adenoidectomy between thickness of adenoids along the line pm ho and the length of dorsal edge of vomer·

$$\frac{\text{ad}_4\text{-ho (A29)}}{\text{pm-ho (A121)}} \times 100 \qquad \text{(A38)}$$

Relationship after adenoidectomy·

$$\frac{\text{ad}_2\text{-ho (A30)} \times 100}{\text{pm-ho (A121)}} \qquad \text{(A39)}$$

Relationship before adenoidectomy between thickness of adenoids along the line pm-ba and the depth of bony nasopharynx

$$\frac{\text{ad}_1\text{-ba (A26)}}{\text{pm-ba (A92)}} \times 100 \qquad \text{(A40)}$$

Relationship after adenoidectomy

$$\frac{\text{ad}_1\text{-ba (A27)}}{\text{pm-ba (A92)}} \times 100 \qquad \text{(A41)}$$

Relationship between area of adenoids and area of bony nasopharynx.

$$\frac{\text{ad}_2\text{-ho-ba-ad}_1\text{-ad}_2}{\text{pm-ho-ba-pm}} \times 100 \qquad \text{(A32)}$$

Relationship between area of adenoids and area of nasopharynx

$$\frac{\text{ad}_2\text{-ho-ba-ad}_3\text{-ad}_1\text{-ad}_2}{\text{pm-ho-ba-ho -pm}} \times 100 \qquad \text{(A35)}$$

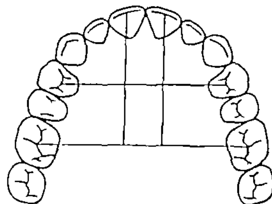


Fig 12 Measuring points for width and length of dental arches. After Lundström.

Measurements on the casts

Impressions of the upper and lower dental arches were taken in Tissuetex" alginate material and plaster models made A wax record in maximum intercuspidation was also taken

The following 14 measurements were made on the models

A. In the upper and lower jaws
1 Width of dental arch between first molars (A49 50) first deciduous molars (A51 52)
2 Length of dental arch (A53 54)
3 The space difference of the dental arch (A61 62)

B In the upper jaw only·
1 Height of palatal vault (A60)

C. Upper and lower dental arches in occlusion.
1 Overjet (A55)
2. Overbite (A56)
3 Molar occlusion (A57 58)

The transverse relation (A59) between the jaws was evaluated on the models without measurements

A 1 The width of the dental arch in the upper jaw was measured (*with an accuracy of* ±0 1 mm) with sliding callipers at the first *molars, and the first* deciduous molars in accordance with Lundström (1948) (see Fig. 12) The width of the dental arch in the lower jaw

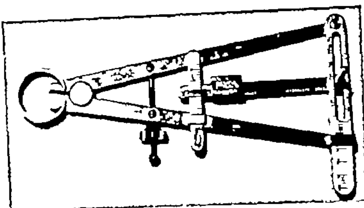


Fig 13 Three-dimensional callipers designed by Korkhaus (and modified by Lundström) for measuring the length of the dental arch and the height of the palatal vault.

was measured in the same way as in the upper jaw

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A 3 The space-difference of the dental arch. The difference between the circumference of the dental arch from second molar to second molar and the sum of the mesodistal diameter of first molar premolars, canines and incisors. The mesiodistal tooth diameter and the space of the dental arch were measured in accordance with Lundström (1948) (see Fig. 14)

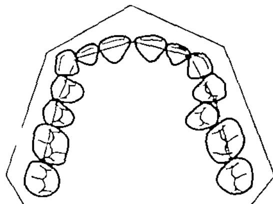


Fig 14 Measuring the space in the dental arch. After Lundström.

B 1 The height of the palatal vault, i.e. to its highest point, was measured at right angles to the plane of occlusion, in the line joining the measuring points on the first molars. The threedimensional compass was used for this measurement as well, placed in the same way as in measurement of the length of the dental arch (see Fig. 15) The measurements were made in accordance with Lundström (1948) with an accuracy of ±0 1 mm.

C 1 The overjet was measured, with an accuracy of ±0 1 mm, at the central incisors, using the sliding callipers. The overjet was taken as the mean of the distance from the midpoint of the edge of the left upper central incisor to the labial surface of the left lower central incisor and of the corresponding distance between the right upper central incisor and right lower central incisor The relevant distance was measured parallel to the plane of occlusion, at right angles to the dental arch (see Fig. 16)

C 2. The overbite was also measured at the central incisors. It is given as the mean of the distance from the edge of the left lower central incisor to the point on its labial surface on which the sliding calipers impinged in measurement of the overjet, and of the corresponding distance on the right lower central incisor A horizontal groove was drawn through this point (see Fig. 16) Using the sliding callipers, the distance was measured with an accuracy of ±0 1 mm. A frontally open bite is denoted by a negative value, and the reverse by a positive value

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$$\frac{\text{ad}_2\text{-ho (A29)}}{\text{pm-ho (A121)}} \times 100 \qquad \text{(A38)}$$

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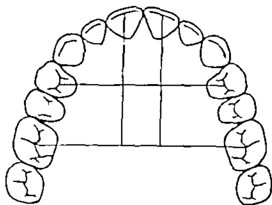


Fig 12 Measuring points for width and length of dental arches. After Lundström.

Measurements on the casts

Impressions of the upper and lower dental arches were taken in "Tissuetex" alginate material and plaster models made. A wax record in maximum intercuspidation was also taken.

The following 14 measurements were made on the models.

A. In the upper and lower jaws

1. Width of dental arch between first molars (A49 50) first deciduous molars (A51 52)
2. Length of dental arch (A53 54)
3. The space difference of the dental arch (A61 62)

B In the upper jaw only

1. Height of palatal vault (A60)

C Upper and lower dental arches in occlusion

1. Overjet (A55)
2. Overbite (A56)
3. Molar occlusion (A57 58)

The transverse relation (A59) between the jaws was evaluated on the models without measurements.

A 1 The width of the dental arch in the upper jaw was measured (with an accuracy of ± 0.1 mm) with sliding calipers at the first molars, and the first deciduous molars in accordance with Lundström (1948) (see Fig. 12) The width of the dental arch in the lower jaw

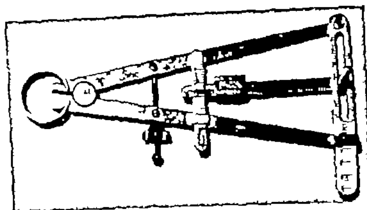


Fig 13 Three-dimensional calipers designed by Korkhaus (and modified by Lundström) for measuring the length of the dental arch and the height of the palatal vault.

was measured in the same way as in the upper jaw

A 2. The length of the dental arch as measured (to within ±0 1 mm) with the three dimensional calipers (compass) designed by Korkhaus and modified by Lundström (see Fig. 13) The measurements were made in accordance with Lundström (1948).

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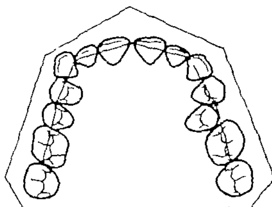


Fig 14 Measuring the space in the dental arch. After Lundström.

B 1 The height of the palatal vault, i.e. to its highest point, was measured at right angles to the plane of occlusion, in the line joining the measuring points on the first molars. The threedimensional compass was used for this measurement as well, placed in the same way as in measurement of the length of the dental arch (see Fig. 15). The measurements were made in accordance with Lundström (1948), with an accuracy of ±0 1 mm.

C 1 The overjet was measured, with an accuracy of ±0 1 mm, at the central incisors, using the sliding calipers. The overjet was taken as the mean of the distance from the midpoint of the edge of the left upper central incisor to the labial surface of the left lower central incisor and of the corresponding distance between the right upper central incisor and right lower central incisor The relevant distance was measured parallel to the plane of occlusion, at right angles to the dental arch (see Fig. 16)

C 2. The overbite was also measured at the central incisors. It is given as the mean of the distance from the edge of the left lower central incisor to the point on its labial surface on which the sliding calipers impinged in measurement of the *overjet*, and of the corresponding distance on the right lower central incisor A horizontal groove was drawn through this point (see Fig. *16*) Using the sliding calipers, the distance was measured with an accuracy of ±0 1 mm. A frontally open bite is denoted by a negative value and the reverse by a positive value.

C 3 The molar occlusion was taken as the

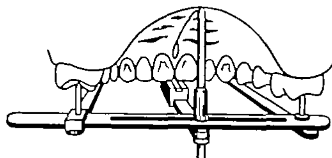


Fig 15 Measuring the height of the palatal vault. After Lundström.

distance between the mesial surfaces of the upper and lower first molars measured in the upper occlusal plane (see Fig. 17) The measurement was performed with the end of the sliding calipers The distance was denoted as positive when the mesial surface of the upper first molar occluded distally to the mesial surface of the lower first molar

The transverse relation between the jaws was studied only concerning the occurrence of lateral crossbite

Indexes for dentition variables measured on casts

In addition to linear measurements on the models, indexes were calculated as percentage values for the relationship between dentition variables for breadth, height and length

The relationship between the width of the lower and upper arches is expressed by variables A63–64 Index values close to 100 denote cusp-to-cusp dentition and higher values cross bite

$$\frac{\text{Arch width } M_1\text{–}M_1 \text{ lower (A50)}}{\text{Arch width } M_1\text{–}M_1 \text{ upper (A49)}} \times 100 \qquad \text{(A63)}$$

$$\frac{\text{Arch width 04–04 lower (A52)}}{\text{Arch width 04–04 upper (A51)}} \times 100 \qquad \text{(64)}$$

The relationship between the length and width of the upper arch is expressed by variable A65

$$\frac{\text{Arch length upper (A53)}}{\text{Arch width } M_1\text{–}M_1 \text{ upper (A49)}} \times 100 \qquad \text{(A65)}$$

The relationship between height of palatal vault and width of upper arch is expressed by variable A66

$$\frac{\text{Height of palatal vault (A60)}}{\text{Arch width } M_1\text{–}M_1 \text{ upper (A49)}} \times 100 \qquad \text{(A66)}$$

Recordings of nasal airflow

The nasal airflow was measured in this investigation according to the method described by Aschan et al (1958) and subsequently modified in minor respects The recordings were made in Örebro using the original apparatus in close collaboration with these authors technicians, who are well acquainted with the method. Together with Bäckström I have previously employed this method for measuring the nasal airflow in mouth breathing 9-year olds (Linder Aronson & Bäckström 1960) The satisfactory results on that occasion justified the use of the method in younger patients as well in order to obtain objective values for the nasal function.

The method involves the simultaneous re

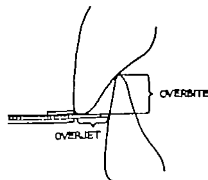


Fig 16 Measuring overjet and overbite

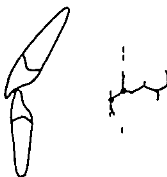


Fig 17 Measuring molar occlusion According to Seipel.



Fig 18 Rhinometry The flow of the expiratory air is measured in plate orifice attached to the nasal mask. The pressure difference between the oral cavity and nasal openings is measured by means of polyethylene tubes in the mouth and mask.

cording of the rate of airflow and of the pressure gradient between the nasopharynx and the nostrils. A mask with insignificant dead space is held over the nose (cf Fig. 18) The pressure gradient is measured between the inside of the mask and a plastic tube introduced into the oral cavity The subject keeps his mouth closed during the recording. Measurements on a subject free from pharyngeal reflexes have shown that the pressure in the oral cavity is practically identical with that in the nasopharynx (Aschan et al., 1958) The rate of flow is obtained by allowing the air to flow into the nose through a venturimeter (gas flow meter) connected to the mask.

The venturimeter consists of a plexiglass tube 10 8 cm long and with an inner diameter of 17.5 mm. A plate orifice 10 0 mm in diameter is fixed in the middle of the tube. Openings on each side of the plate orifice are connected by means of polyethylene tubes to both sides of a manometer The pressure difference between the two openings provides a measure of the airflow along the tube.

The pressure difference between the mouth and the mask was measured by means of polyethylene tubes connected to another manometer The measuring apparatus has been described by Drettner (1961) as follows:

"The two manometers for the estimation of flow and pressure were of the same construction but of different sensitivity Each manometer consisted essentially of a brass membrane, which acted as a mobile plate of a double capacitor Parallel with each of the capacitors were coils connected to resonance circuits which were supplied from an oscillator with a frequency of 425 Kc/sec. With displacements of the brass membrane, the tuning in the two resonance circuits was changed in the opposite direction. Signals from the resonance circuits were led into a differential amplifier with a symmetric input. After amplification and demodulation, the signal was passed into the DC-input of a double channel Elema mingograph model 24 The flow variations were recorded on the upper channel, and the differential pressure variations on the lower The response time for full deflection was the same for flow and differential pressure amounting to about 0 1 sec as measured with a rapidly appearing high flow of pressure The paper speed of the mingograph during recordings was 5 cm/sec.

The mingograph records (Fig. 19) contained the continuous recordings of the airflow through the nose (lit/min) and the differential pressure between the nasopharynx and the nostrils (mm H_2O) The recordings above the base line represent expiration, and those below the base line

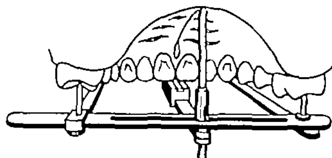


Fig 15 Measuring the height of the palatal vault. After Lundström.

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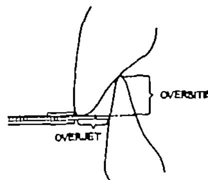


Fig 16 Measuring overjet and overbite

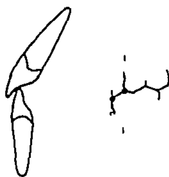


Fig 17 Measuring molar occlusion. According to Seipel.

CHAPTER 4

Error of methods

When assessing the error of the method, consideration must be paid to regular as well as irregular errors. Errors of method are presented below for

1 Anamnesis variables
2. Adenoid, dentition, skeleton and lip variables
3 Airflow variables
4 Variables for tongue position

1 ANAMNESIS VARIABLES

An otologist and the author made double determinations in every child of the anamnestic data A04 (Mode of breathing) A05 (Mouth open or closed in sleep), A06 (Recurrent infections in ear nose and throat), A07 (Allergy), A08 (Previous adenoidectomy), A09 (Siblings with ear nose and throat diseases)

In the case of the adenoidectomy children, the author had access to the otologist's report. The assessment of the controls, however was undertaken entirely independently by the otologist and the author The results are presented in Tables 2 and 3

As indicated by the tables, the results of the double determinations were much the same for the operated children and the controls. It therefore seems that the author's assessments were not substantially affected by having access to the otologist's records for the adenoidectomy children.

The greatest discrepancy (10–11 %) between the two assessments occurs in both groups for variable A06, Recurrent infections in the ear nose and throat. In both groups the deviation is of a regular nature in that the otologist noted recurrent infections in twice as many cases as the author

The assessments of other anamnestic data display good agreement between the otologist and the author.

2. ADENOID DENTITION, SKELETON AND LIP VARIABLES

Double determinations in the same child have been compared in the case of measurements on pairs of radiographs taken on the same occasion, double measurements on casts and

Table 2. *Double determinations of anamnestic data in the adenoidectomy children*

Variable	N	Assessments by otologist and the author			
		Same		Different	
		n	%		%
A04 Mode of breathing	81	79	98	2	2
A05 Sleeps with mouth open or closed	81	77	95	4	5
A06 Recurrent infections	81	72	89	9	11
A07 Allergy	81	75	93	6	7
A08 Previous adenoidectomy	81	77	95	4	5
A09 Siblings with ear nose & throat diseases	81	78	96	3	4

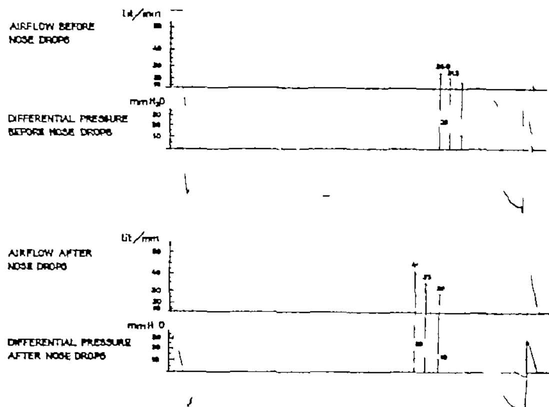


Fig 19 Recording of the airflow through the nose (lit/min) and the pressure difference between the oral cavity and the nasal openings (mm H_2O) during nasal respiration. The base line represents the zero value and the section above the base line represents expiration. Flow was measured at pressure differences of 10 15 and 20 mm H_2O before and after nose drops.

inspiration As the response time was the same for airflow and pressure recordings, corresponding points on the same respiration section could be used to measure flow and pressure difference at a certain moment of the respiration. The airflows have been measured on the expiration section of the curve at pressure differences of 10 15 and 20 mm H_2O

Two recordings were made, one after the child had adapted to the climate in the examination room for about 45 minutes and the other about 15 min after inducing decongestion of the nasal mucosa by spraying a dose of 0.5 mg/ml oximetazolin chlorid (Nesenl®) into the nostrils The latter recording provided an estimate of the anatomic resistance and the former an estimate of the physiological degree of swelling of the nasal mucosa.

Table 5 *Error of method for measurements of airflow before and after nose drops*

S.D which represents the variance of the difference *d* between an initial value and value obtained one month later is calculated from the formula $\Sigma(d_i-\bar{d})^2/(N-1)$, where *d* is this difference for child *i*, $\bar{d}$ is the mean of the differences and *N* is the number of double determinations.

$\frac{S.D}{2}$ is an estimate of the variance in the irregular error of individual determinations.

$\sigma^{**}=\Sigma d^2/N$ which is an estimate of the variance of the error in single measurements if there are no regular differences between measurements on different occasions.

S^2_{tot} is the variance in all the children in the study on the initial occasion

Variable		Mean (controls) Initially	One month later	Diff.	S.D	$\frac{S.D}{2}$	σ^{**}	S^2_{tot}	$\frac{S.D}{2}$ in % of S^2_{tot}
A67 resp. A73 airflow before nose drops	50	18.79	18.65	0.14	16.72	8.36	8.20	27.41	30
A70 resp. A76 airflow after nose drops	50	25.56	26.97	−1.41	29.35	14.68	15.38	59.97	28

this is a cross-section rather than a longitudinal study the error of method should be seen in relation to the interindividual variation on a particular occasion. The size of the error in relation to the intraindividual variation between different occasions is therefore irrelevant here.

3 AIRFLOW VARIABLES

Airflow measurements in the same child at one month's interval were compared for the fifty controls for whom such data were obtained at 10, 15 and 0 mm H_2O As measurements at these differential pressures display a very high intercorrelation ($r > 0.97$) only the error of method for airflow measurements at a differential pressure of 10 mm H_2O before (A67) and after (A70) nose drops will be considered here

It will be seen from Table 5 that the error variance (**) for individual measurements is only slightly different from the irregular error in the individual determination (S.D /2) This indicates that there is no remarkable regular error between the airflow measurements obtained on the two occasions one month apart. Nor was any such difference expected, as one

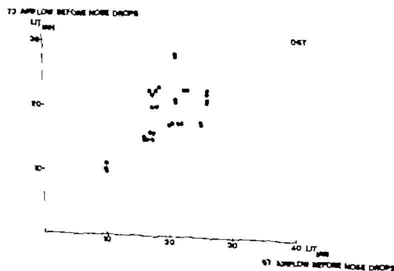


Fig 20 Correlations between measurements of airflow (lit/min.) before nose drops I 69 controls at the *first* (A67) and second (A73) examinations.

Table 3 *Double determinations of anamnestic data in the controls*

Variable	N	Assessments by otologist and the author			
		Same		Different	
		n		n	
A04 Mode of breathing	81	77	95	4	5
A05 Sleeps with mouth open or closed	81	76	94	5	6
A06 Recurrent infections	81	73	90	8	10
A07 Allergy	81	77	95	4	5
A08 Previous adenoidectomy	81	81	100	0	0
A09 Siblings with ear nose & throat diseases	81	78	96	3	4

clinical measurements made on two occasions with an interval of one month

The double determinations were made on twenty children selected at random from the 162 children and concerned all the variables registered in the form of measurements The sum of regular and irregular errors was calculated with the formula for the variance of errors of method $\sigma^{*2} = \frac{\Sigma d^2}{2N}$ where d is the difference between two measurements and N is the number of double determinations

In order to assess the importance of the error of method the error variance (σ^{*2}) was studied in relation to the variance for all the 162 children (S^2_{162})

It was found that, with the exception of the variables listed in Table 4 the error variance amounted to less than 3% of the total variance for each variable

This means that for the majority of variables, the error of method is of little importance compared with the biological variation

In the case of variables for which the error variance is greater than 3% of the total variance there is a risk in simple correlation analyses that the size of the true correlations with other variables will be underestimated

The same applies to regression coefficients for these variables though here the error may involve an overestimation

From the last column in Table 4 it will be seen that no variable has an error variance of more than 10% of the total variance and that the largest error is for an angle measurement, namely A45 The angle between the occlusal and the nasion-sella lines

The error of method for the adenoid dentition skeleton and lip variables is only of secondary importance in the present context Since

Table 4 *Variables for which the variance of the error of method > 3 of the variance in all the children*

σ^{*} is an estimate of the variance of the error of method in mm for individual measurements on different occasions, determined from double determinations according to the formula $\Sigma d^2/2N$ where d is the difference between two occasions and N is the number of double determinations. S^2_{162} represents the variance in all the children in the study

Variable	N	σ^{*2}	S^2_{162}	σ in % of S^2_{162}
A30 ad_1–ho postop	20	0.41	9 95	4 12
A42 ps, sm on OL	20	0.40	7 10	5 63
A45 OL/NSL	20	1 21	13.37	9.05
A82 Nose width over alae nasi	20	0 17	3 89	4 37
A83 Nose width above alae nasi	20	0 17	2.64	6.43
A86 s–ba	20	0.46	8.87	5 18
A93 bo ⊥ pm–ba	20	0.18	3 09	5 82
A96 Height of upper lip	20	0.39	4 91	7 94
A100 bch–bch	19	0.24	5 18	4 63
A121 pm–ho	20	0.38	4 69	8.10
A122 ba–ho	20	0.48	5.83	8.23

Table 5 *Error of method for measurements of airflow before and after nose drops*

S.D which represents the variance of the difference d between an initial value and value obtained one month later is calculated from the formula $\Sigma(d-\bar{d})^2/(N-1)$, where d is this difference for child i, $\bar{d}$ is the mean of the differences and N is the number of double determinations.

$\frac{S.D}{2}$ is an estimate of the variance in the irregular error of individual determinations.

σ^{*2} $\Sigma d^2/N$ which is an estimate of the variance of the error in single measurements if there are no regular differences between measurements on different occasions.

S^2_{tot} is the variance in all the children in the study on the initial occasion

Variable		Mean (controls) Initially	One month later	Diff	S.D	$\frac{S.D}{2}$	σ^{*2}	S^2_{tot}	$\frac{S.D}{2}$ in % of S_{tot}
A67 resp. A73 airflow before nose drops	50	18.79	18.65	0.14	16.72	8.36	8.20	27.41	30
A70 resp. A76 airflow after nose drops	50	25.56	26.97	−1.41	29.35	14.68	15.38	59.97	28

this is a cross-section rather than a longitudinal study the error of method should be seen in relation to the interindividual variation on a particular occasion. The size of the error in relation to the intraindividual variation between different occasions is therefore irrelevant here.

3 AIRFLOW VARIABLES

Airflow measurements in the same child at one month's interval were compared for the fifty controls for whom such data were obtained at 10 15 and 20 mm H_2O As measurements at these differential pressures display a very high intercorrelation ($r > 0.97$) only the error of method for airflow measurements at a differential pressure of 10 mm H_2O before (A67) and after (A70) nose drops will be considered here

It will be seen from Table 5 that the error variance (σ^{*2}) for individual measurements is only slightly different from the irregular error in the individual determination (S.D /2) This indicates that there is no remarkable regular error between the airflow measurements obtained on the two occasions one month apart. Nor was any such difference expected, as one

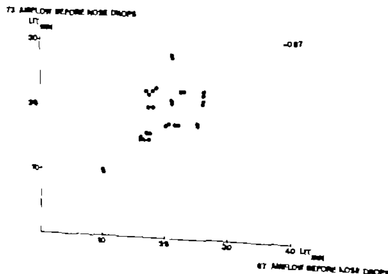


Fig 20 Correlations between measurements of airflow (lit/min.) before nose drops in 69 controls at the first (A67) and second (A73) examinations.

Table 3 *Double determinations of anamnestic data in the controls*

Variable	N	Assessments by otologist and the author			
		Same		Different	
		n		n	%
A04 Mode of breathing	81	77	95	4	5
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A06 Recurrent infections	81	73	90	8	10
A07 Allergy	81	77	95	4	5
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clinical measurements made on two occasions with an interval of one month.

The double determinations were made on twenty children selected at random from the 162 children and concerned all the variables registered in the form of measurements The sum of regular and irregular errors was calculated with the formula for the variance of errors of method $\sigma^{*2} = \frac{\Sigma d^2}{2N}$ where d is the difference between two measurements and N is the number of double determinations

In order to assess the importance of the error of method the error variance (σ^{*2}) was studied in relation to the variance for all the 162 children (S^2_{162})

It was found that, with the exception of the variables listed in Table 4 the error variance amounted to less than 3% of the total variance for each variable

This means that for the majority of variables the error of method is of little importance compared with the biological variation

In the case of variables for which the error variance is greater than 3% of the total variance there is a risk in simple correlation analyses that the size of the true correlations with other variables will be underestimated

The same applies to regression coefficients for these variables though here the error may involve an overestimation

From the last column in Table 4 it will be seen that no variable has an error variance of more than 10% of the total variance and that the largest error is for an angle measurement, namely A45 The angle between the occlusal and the nasion-sella lines

The error of method for the adenoid, dentition, skeleton and lip variables is only of secondary importance in the present context Since

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σ is an estimate of the variance of the error of method in mm for individual measurements on different occasions, determined from double determinations according to the formula $\Sigma d^2/2N$ where d is the difference between two occasions and N is the number of double determinations. S^2_{162} represents the variance in all the children in the study

Variable	N	σ^{*2}	S^2_{162}	σ^* in of S^2_{162}
A30 ad_r–ho postop	20	0.41	9 95	4 12
A42 ss, sm on OL	20	0 40	7 10	5 63
A45 OL/NSL	20	1.21	13.37	9 05
A82 Nose width over alae nasi	20	0.17	3 89	4 37
A83 Nose width above alae nasii	20	0 17	2.64	6.43
A86 s–ba	20	0.46	8 87	5 18
A93 ho ⊥ pm–ba	20	0.18	3.09	5.82
A96 Height of upper lip	20	0.39	4 91	7 94
A100 bch–bch	19	0.24	5 18	4 63
A121 pm–ho	20	0.38	4 69	8.10
A122 ba–ho	20	0.48	5 83	8.23

Table 6. *Autocorrelations between the residuals when the children are arranged in time sequence*

Residuals obtained as the difference between observed values and values predicted by the regression equation (these equations are given on p. 129). Dependent variables: airflow measured t a differential pressure of 10 mm H_2O before and after nose drops preoperatively (A 67 and A 70 respectively) and postoperatively (A 73 and A 76). correlation between consecutive residuals correlations between residuals one, two and three individuals apart respectively

Variable				
A67 Preop. airflow before nose drops	−0.03	0.04	0.13	−0.05
A70 Preop. airflow after nose drops	−0.04	0.12	0.09	−0.03
A73 Postop. airflow before nose drops	−0.03	−0.07	0.01	−0.06
A76 Postop. airflow after nose drops	0.10	−0.01	0.07	0.03

the mask may also have affected the swelling of the nasal mucous membrane. Errors of application and varying reactions to the instructions for airflow recordings presumably account for an essential part of the error of method

(c) *Calibration errors*

The measuring apparatus was calibrated several times for pressure differences and flow during the course of the study The calibrations proved to be almost constant. They were performed at the Laboratory of Physiological Climatology Akademiska Sjukhuset, Uppsala, in accordance with the procedure described by Drettner (1961).

Since the calibrations were undertaken only sporadically the regular error may have changed successively between calibrations. If this was the case, one would expect to find a positive correlation between the regular errors after two consecutive measurements. If one measurement displays a pronounced regular error it is thus to be expected that the next measurement will do the same

This matter was investigated by calculating autocorrelations for the present data.

Although it is not possible, however to measure the regular error directly one can calculate so-called residuals in the manner adopted in this study Having obtained the differences between observed values and values predicted in accordance with the regression equation, the residuals are arranged in time sequence and autocorrelations are calculated for consecutive residuals. A study of these correlations will show whether there is a consistent change in the regular errors

As will be seen from Table 6, all the autocorrelations are low Thus, no regular apparatus errors resulting in successive changes in the regular error between calibrations could be detected. The absence of autocorrelations between the residuals also indicates that there are no remarkable regular shifts as a result of the investigator's instructions and application of the apparatus for recording airflow

(d) *Actual changes in individuals between the first and second measurements*

It is conceivable that the nasal mucosa changed between the first and second measurement owing to the start or end of an infection, a change in climate or the like If such factors affected the nasal mucosa, their effect would be modified to some extent by nose drops. On the other hand, nose drops themselves may conceivably increase the variation from time to time to some extent.

According to Table 5 the error variances for variables A67 and A70 i.e. airflow before and after nose drops, bear almost the same relation to the variance for the total material, namely 30 and 28% respectively

Since the error of method is only slightly reduced by nose drops, the change in nasal mucosa was probably small between the first and second recordings.

A76 AIRFLOW AFTER NOSE DROPS LIT/MIN

A70 AIRFLOW AFTER NOSE DROPS LIT/MIN

0,75

Fig 1 Correlations between measurements of airflow (lit/min.) after nose drops in 69 controls at the first (A70) and second (A76) examinations.

month is too short an interval for any substantial biological changes in healthy subjects.

The variance of the irregular error in a single determination ($S D^2/2$) is large in relation to the mean as well as to the variance for all 162 individuals on the first occasion. This is also indicated by the correlations between airflow data in the controls on the first and second occasions for which the coefficients amounted to no more than 0 67 ($N = 69$) and 0 75 ($N = 69$) for airflow before and after nose drops respectively (see Figs 20 and 21)

Airflow is treated as a dependent variable in this study and consequently it is important to analyze the predictive value of different factors for the variance displayed by airflow An important factor in this respect is the error of method which may comprise (*a*) apparatus errors, (*b*) errors of application and instruction (*c*) calibration errors and (*d*) actual changes in the individual between the first and second recordings.

(a) Apparatus errors

The error of method for the apparatus was analyzed in model tests in which the relationship between flow and pressure difference was studied on rubber models of the nose reproduced from a post mortem impression of human nasal cavities and epipharynx (Drettner 1961) The error of method of the apparatus was calculated to ± 1 3 lit/min for an airflow of 39 8 lit/min measured at a differential pressure of 10 mm H_2O (Drettner 1961)

(b) Errors of application and instruction

The nose mask belonging to the apparatus was fitted in different ways according to the facial type of the child As the same mask was used for all the children, it is possible that leakage occurred between the edge of the mask and the face It is also conceivable that mechanical pressure from the mask around the nose altered the degree of swelling of the nasal mucous membrane in some cases. The recording sometimes took longer than usual if the child misunderstood the instructions and consequently failed to cooperate, for instance by sucking through the mouth tube or closing off communication between mouth and epipharynx with the tongue In such cases, the accumulation of warm, moist air in the dead space of

The cineradiographs were analyzed in a viewer for 35 mm film (Arnoe Corp., Copenhagen) (Jensen, 1968) and tracings of single frames were made with the film projected on a translucent screen.

The position of the tongue during the three exposures in each individual was drawn on tracing paper and judged in relation to a line passing through the distal surface of the most distal upper molar perpendicular to a line through the contour of the floor of the nose (see Fig. 22). This assessment was made by the author together with an orthodontist well acquainted with cineradiographic analysis. Such tracings were made on three different occassions from each of the series of pictures from the three exposures.

The results show that the tongue is held considerably lower in mouth breathing than in nose breathing. The tongue was held highest during the second exposure (nose breathing with the mouth open) This is natural since, with the mouth open, the tongue is held against the soft palate to achieve breathing through the nose alone It is particularly noteworthy that the position of the tongue remained unchanged throughout each of the three exposures with the exception of two cases in which it moved somewhat during the first exposure (nose breathing with the lips closed)

Exact measurements of tongue position during the exposures were not attempted in view of the difficulty of determining whether observations during forced mouth breathing also apply to persons who breath through the mouth on account of nasal obstruction.

The good stability of tongue position during 5 sec cineradiography strengthens the reliability of assessments of tongue position in nose breathers and mouth breathers simply by studying lateral radiographs.



Fig 2 Cineradiographic photographs and tracings of tongue position during (a) nose breathing with mouth closed, (b) nose breathing with mouth open, and (c) mouth breathing.

4 VARIABLES FOR TONGUE POSITION

Double determinations of tongue position in relation to the hard and soft palates were made on lateral radiographs in the same way as for the adenoid skeleton and lip variables. The error variance amounted to less than 5% of the total variance

In order to assess how stable the position of the tongue is between lateral radiographs taken at intervals of a few seconds tongue position was also filmed cineradiographically for 5 sec This was done with the type of film and apparatus described by Jensen (1968) The films were taken at a frequency of 24 frames per second

Cineradiographs were taken in 8 students with normal occlusion, three exposures lasting 5 sec each being made in each individual

During the first exposure the subject breathed through the nose held the lips closed and kept the lower jaw in the rest position

During the second exposure conditions were the same as for the first except that the mouth was kept *open*.

During the third exposure the subject breathed through the mouth alone with the lower jaw in a resting position

performed with x and as regressors and using the equation $y = a + bx + cz$, it will be found that the coefficient in front of x i.e. $b =$ 0.000 This regression coefficient expresses the effect of variable x on y when allowance is made for z. In the present case, the regression coefficient indicates that x has no effect.

Briefly then, a simple correlation or regression analysis does not always give the same result as a partial or a multiple regression analysis.

Furthermore, it should be noted that a regression coefficient must also be interpreted in the light of the other variables included in the regression analysis. In other words, an analysis will depend upon which variables are included. Consequently the *selection of regressors* is of major importance. In particular one should try to avoid including regressors that are causally influenced by the regressand. The regressors which occur in the present study can thus be regarded either as conceivable causes of the regressand or as symptoms of an underlying variable with a conceivable causal effect on the regressand

In the case of certain regressands, the number of possible regressors exceeded the capacity of the computer programme. In such cases the regressors that did not show a significant simple correlation with the regressand were excluded and in this way the number of regressors in the regression analyses never exceeded 68

The regression analyses that are described in greater detail have only a few regressors for which partial correlation and regression coefficients are reported This is because only regressors significant at the 5% level have been included.

Stepwise regression analyses have been performed. This means that the regressor with the strongest positive or negative correlation with the regressand is introduced first, after which one introduces the regressor that shows the strongest partial correlation to the regressand with allowance for the first regressor and so on.

A list of the sequence in which the regressors were introduced is given in connection with the regression analyses. With this stepwise procedure the analysis is discontinued when the regressor to be introduced next does not reach the requisite level of significance.

R^2 (the square of the multiple correlation coefficient) indicates how large a part of the regressand's variance can be attributed to the regressors (see Appendix, p 128)

If $R^2 = 0$ nothing of the variance can be attributed to the regressors, while if $R^2 = 1$ then all the variability is attributable to the regressors. Obviously it is desirable to have a high value for R^2 In this study values of R^2 < 0.30 are regarded as weak, while $R^2 > 0.50$ is considered satisfactory

Weak values of R^2 may be a consequence of a large error of method for the regressand (cf. the discussion with A67 and A70 as regressands, pp 88, 89) They may also indicate that essential variables have not been registered. No additional variables of importance were discovered, however in the course of a study of large residuals.

Another reason for low values of R^2 may be that several measurements are lacking for certain variables, particularly those connected with the dentition and airflow (in the case of dentition variables, children who were changing from deciduous to permanent teeth, in the case of airflow variables, children who had *difficulty* in managing the nasal airflow apparatus)

Finally it should be mentioned that R^2 is sometimes low when only regressors with significant correlation coefficients are included but rises substantially when other regressors are taken into account.

Concerning values of $R^2 > 0.50$, it should be noted that these may be relatively high as the regressors involved serve as indicators of the same condition as the regressand

If only two variables x and y are studied, then $r^2(xy) = R^2$ In the above example where $r = -0.30$ R^2 amounts to only 0.09 i.e. a very low determinative value even though the correlation coefficient shows a high level of

Methods for analyzing relationships

The relationships between variables have been studied with the aid of simple correlation analysis and multiple regression analysis. The formulas employed are reported in the appendix Statistical methods. The following is a brief account of what these methods of analysis involve and why and how they were performed.

Let us start with a *simple correlation* between the variables x and y. This gives an indication of the relationship between x and y without taking other variables into account. In order to see what happens when the correlations of other variables to x and y are also considered, one can perform partial correlation analysis or multiple regression analysis.

The value of *partial correlation analysis* is illustrated by the following example, in which three variables—x, y and z—symbolize airflow (A67), mouth breathing (A15) and size of adenoids (A20) respectively.

Between x and y the correlation coefficient $r = -0.30$, which is highly significant ($P < 0.001$). This correlation tells us that mode of breathing and airflow are related and that airflow is lower on the average for mouth breathers than nose breathers.

We can then investigate whether this relationship is entirely due to adenoids obstructing the airflow and consequently increasing the propensity to breath through the mouth. The correlation coefficient between x and z is $r = -0.45$, suggesting that airflow is inhibited by size of adenoids, while the correlation between y and z is $r = 0.66$, indicating that mouth breathing is more common among the children whose adenoids are large.

Thus we have found that $r(xy) = -0.30$, $r(xz) = -0.45$ and $r(yz) = 0.66$. The relationship between two variables when a third variable is kept *constant* is expressed by the partial correlation, which is calculated according to the formula

$$r(xy.z) = \frac{r(xy) - r(xz)\, r(yz)}{\sqrt{(1 - r^2(xz))(1 - r^2(yz))}}$$

Substituting our correlations in this formula gives $r(xy.z) = -0.01$. This implies that the relationship between mouth breathing and airflow is entirely attributable to these variables' relationship with size of adenoids. In other words, if allowance is made for size of adenoids the relationship between mode of breathing and airflow as measured by the correlation coefficient is almost equal to 0.

In this example it is more interesting to learn that the relationship between x and y is entirely attributable to z than simply to learn that x and y display a negative correlation.

Partial correlation analysis can be extended to cover more than one variable in addition to x and y. Thus one can study the relationship between x and y while making allowance for the k variables $z_1, z_2, \ldots, z_k$. It is partial correlation coefficients of this type that are reported in the tables for the regression analyses.

The change in the strength of a relationship that can be detected by extending a simple correlation to a partial correlation has its counterpart in an extension from *simple regression* to *multiple regression*. Suppose that in a regression analysis of the present data, y = A15 (Mouth breathing) is chosen as the regressand and x = A67 (Airflow) as the regressor. Using the equation $y = A + Bx$ one obtains the regression coefficient $B = -0.028$, which differs significantly from 0 ($P < 0.001$).

If instead a multiple regression analysis is

CHAPTER 6

Results of comparisons between the adenoidectomy and control groups and of simple correlation analyses

The first part of this chapter presents in separate sections the variable groups for anamnesis, dentition, adenoids, airflow skeleton & lips and tongue position respectively The definitions of the variables featured in the tables will be clear from the list of variables in Table 1 pp 13–15 In each section percentages, means and standard deviations are reported separately for each of the three control groups (classified by radiographic size of adenoids) and the two adenoidectomy groups (classified by the indication for operation. recurrent otitis media or nasal obstruction) The standard deviations are of interest, in that, for instance, they indicate the degree of overlapping between the groups

The other part of the chapter is devoted to simple correlations between variables belonging to the same group as well as between variables belonging to different variable groups. Correlation coefficients are shown specifically in the tables only if they are significant at the 1% level Furthermore, in view of the strong intercorrelations displayed by the airflow measurements at differential pressures of 10, 15 and 20 mm H_2O ($r > 0.97$) only airflow at 10 mm H_2O has been included in the tables of correlations between the airflow variables and other variables

In order to avoid making the analysis of results unnecessarily repetitive, the presentation in this chapter is purely descriptive. Discussions of the results will be found in the next chapter together with the presentation of results from the multiple regression analyses.

COMPARISONS BETWEEN THE ADENOIDECTOMY AND CONTROL GROUPS

Anamnesis and clinical status variables

The percentage incidences for certain anamnestic variables and certain clinical status variables defined in accordance with Table 1 are presented in Table 7

Only one definition has been altered from Table 1 namely concerning variable A04 Mode of breathing, in that the category "breathing through both nose and mouth has been dropped. The children who reported that they breathed in this way are included in Table 7 with those who breath through the mouth, which clarifies the criteria for nose breathing.

Standard deviations can be calculated from the data provided in the table using the formula

$$\sqrt{\frac{n}{n-1}p(100-p)}$$

where p is the observed percentage

For all variables the number of observations amounts to 162. The occurrence of significant differences at the 1% or 0.1% level between any pair of groups is noted in the last column of the table The group with the largest percentage has been compared with the group or groups with smaller percentages.

Groups 1 2 and 3 comprise unoperated controls, while the adenoidectomy children make up groups 4 and 5

From Table 7 it will be seen that the percentage distribution by sex is much the same

significance ($P < 0.001$) The example also shows that an analysis of the significance of the correlation coefficients should include information on the coefficient of determination

A very large number of variables has been included in the present study (cf Table 1) Many of them were not expected to display particularly strong correlations with the regressands investigated namely adenoid, airflow and dentition variables They were simply included as a means of exposing any unexpected correlations This *exploratory* approach was adopted since there does not appear to be any means of specifying which set of regressors will give rise to values of $R^2 > 0.50$

This exploratory approach however involves a risk of obtaining artefact significant coefficients To guard against this, a comparison has been made between the number of significant analyses observed and expected at the 5% 1% and 0 1% levels (see Table 53, p 115)

Data processing

All calculations in this study have been performed on the UDAC (Uppsala) computer CDC 3600

The Interest Programme at UDAC was employed in the calculations for *simple correlation analyses means standard deviations, etc.*

The *regression analysis* programme used in the processing of data as described above was taken from Thornber (1966)

in all groups with the exception of group 3 which however consists of only 11 children. It will also be seen that the sex distribution in the total material is 40% girls and 60% boys (by definition, girl = 1 and boy = 0 cf. Table 1)

The percentages for almost all the variables in Table 7 for the unoperated children (i.e. for groups 1 2 and 3 combined) are considerably lower than for the adenoidectomy children (i.e. groups 4 and 5 combined) Variable A10, Prolonged fingersucker is an exception, group 5 having the smallest percentage and group 3 the largest.

Group 1 has very low percentages for the majority of variables, though it is worth noting that even in this group there are children who sleep with their mouth open (A05 8%) or who otherwise have their mouth open (A12, 5%)

Group 2 displays the same tendencies as group 1

The percentages for group 3 Unoperated children with large adenoids, are considerably higher than in group 1 for several variables.

The adenoidectomy children (groups 4 and 5) display a high incidence of mouth breathing, the figures for variables A04 and A15 being 90–95% in group 5 and 57–71% in group 4

The different percentages for the unoperated and the adenoidectomy groups can hardly be explained by discrepancies in the procedure for investigating their anamnesis.

When assessing the anamnesis of all the adenoidectomy children, the author had access to the otologist's report with the same anamnestic data (see Table 2, p. 27) In the case of the unoperated controls, on the other hand, the anamnesis was assessed entirely independently by an otologist and the author (see Table 3 p 28) If the two assessments did not agree (see Tables 2 and 3 pp. 27–28), the author's was adopted.

The data on clinical states represented by variables A12–15 are derived from examinations by the author while those represented by variables A16–19 have been provided by an otologist. The unoperated controls were assessed by one of two otologists and the adenoidectomy children by one of six otologists.

There is a large number of significant differences between groups, in the first place between groups 4 and 5 on the one hand and groups 1 2 and 3 on the other In the case of variables A08 A11 A15 and A16, the inter group differences are a consequence of the group definitions (see p. 12).

Concerning mode of breathing (A04 A15) mouth in sleep (A05), recurrent infections in the ear nose and throat (A06) open or closed mouth (A12) and enlarged adenoids (A16) the differences between groups 4 and 5 in relation to groups 1 2 and 3 are in line with what one would expect, viz. that the incidences of mouth breathers, of recurrent infections in the ear nose and throat and of enlarged adenoids are highest in the adenoidectomy groups.

Furthermore, one might expect that for the variables with differences between adenoidectomy and control groups, group 3 would occupy an intermediate position between groups 4 and 5 and groups 1 and 2. This appears to be the case for mode of breathing (A04), open or closed mouth (A12) obstructed nose breathing (A13–14) and enlarged adenoids (A16) On the other hand, group 3 has a higher percentage—though not significantly higher—than any other group for number of siblings with ear nose and throat diseases (A09) and incidence of prolonged finger suckers (A10). Neither does group 3 differ significantly from group 1 and group 2 in any of the other variables listed in Table 7 Nor are there any significant differences between groups 1 and 2.

Group 5 has significantly higher percentages than group 4 ($P < 0.01$) for mouth in sleep (A05), open or closed mouth (A12), obstructed nose breathing (A13–14) and mouth breathing (A15) Obstructed nose breathing is particularly frequent in group 5 These differences are to be expected since nasal obstruction was the indication for adenoidectomy and served as the basis for the definition of group 5

Table 7 *Percentage frequence of variables concerning anamnesis and clinical status in the five groups of children*

A total of 162 observations were obtained for all variables. Significant differences ($P < 0.01$) between the groups are listed in the last column (the group with the highest percentage has been compared with the group or groups that had smaller percentages)

Variable	Total %	Group 1 Controls No adenoids n = 37 %	Group 2 Controls Small adenoids n = 33 %	Group 3 Controls Large adenoids n = 11 %	Group 4 Adenoid-ectomy otit. med. n = 1	Group 5 Adenoid-ectomy Nasal obstr n = 60 %	Significant differences $P < 0.01$
	Anamnestic data						
A03 Girl = 1	40	41	33	55	43	38	
A04 Mouthbreathing = 1	48	3	3	9	71	95	4 vs. 1 5 vs. 1 4 vs. 2, 5 vs. 2, 4 vs. 3 5 vs. 3
A05 Mouth open in sleep = 1	47	8	12	9	57	93	4 vs. 1 5 vs. 1 4 vs. 2, 5 vs. 2, 4 vs. 3 5 vs. 3 5 vs. 4
A06 Infections in ear nose & throat = 1	40	5	6	0	67	78	4 vs. 1 5 vs. 1 4 vs. 2, 5 vs. 2 4 vs. 3 5 vs. 3
A07 Allergy = 1	4	3	3	0	0	7	
A08 Previous adenoidectomy = 1	4	0	0	0	5	10	
A09 Sibling's ear nose & throat disease = 1	15	3	9	36	29	18	5 vs. 1
A10 Prolonged finger-sucker = 1	12	14	15	27	14	7	
A11 Previous orthodontic therapy = 1	2	0	0	0	5	3	
	Clinical assessments						
A12 Open mouth = 1	42	5	3	18	52	87	4 vs. 1 5 vs. 1 4 vs. 2, 5 vs. 2, 5 vs. 3 5 vs. 4
A13 Obstructed nose breathing left = 1	33	0	9	27	4	72	5 vs. 1 5 vs. 2, 5 vs. 3 5 vs. 4
A14 Obstructed nose breathing right = 1	31	0	6	18	29	67	4 vs. 1 5 vs. 1 5 vs. 2, 5 vs. 3 5 vs. 4
A15 Mouthbreathing = 1	41	0	3	0	57	90	4 vs. 1 4 vs. 2, 4 vs. 3 5 vs. 1 5 vs. 2, 5 vs. 3 5 vs. 4
A16 Enlarged adenoids = 1	51	0	3	18	100	100	4 vs. 1 4 vs. 2 4 vs. 3 5 vs. 1 5 vs. 2, 5 vs. 3
A17 Large tonsils = 1	6	0	0	9	0	15	5 vs. 1 5 vs. 2, 5 vs. 3 5 vs. 4
A18 Swollen nasal mucosa = 1	7	0	6	9	10	12	5 vs. 1
A19 Septum deviation = 1	2	0	0	0	5	3	

Table 9 *Mean (M) and standard deviation* (S.D.) *of dentition variables for the children in the five groups*

The number of children (n) is indicated for variables with a drop-out of more than 10%, i.e. if N < 145. Significant differences (P < 0.01) are listed in the last column (the group with the higher mean has been compared with the group or groups with lower means)

Variable		Total	Group: 1 Controls No adenoids = 37	2 Controls Small adenoids = 33	3 Controls Large adenoids = 11	4 Adenoidectomy Oth. med. = 21	5 Adenoidectomy Nasal obstr. = 60	Significant differences P < 0.01
A42 m & sm projected on OL N 158	M	−0.59	−0.90	−0.01	0.16	−0.87	−0.99	
	S.D.	2.66	2.86	2.13	1.83	2.54	2.94	
A43 Freeway space prop. N 90	M	8.71	6.74	9.96	3.57	9.07	10.03	
	S.D.	14.05	10.81	16.64	1.07	13.90	15.82	
		90	21	16	6	10	37	
A44 OL/ML N 158	M	15.84	14.97	15.41	15.10	14.58	17.15	5 vs. 4
	S.D.	3.90	3.94	3.68	2.82	3.13	4.10	
A45 OL/NSL N 158	M	19.32	17.64	19.94	18.20	18.76	20.39	5 vs. 1 2 vs. 1
	S.D.	3.66	3.03	3.22	3.07	3.62	3.96	
A46 IL_u/NSL N 113	M	102.70	106.70	101.84	101.63	103.57	100.07	1 vs. 5
	S.D.	6.89	4.07	7.23	7.71	7.37	7.01	
		113	31	19	4	15	44	
A47 IL_u/IL_l N 113	M	129.65	125.39	126.85	128.38	128.23	134.47	5 vs. 1 5 vs. 2
	S.D.	9.23	5.95	6.60	9.78	9.44	10.12	
		113	31	19	4	15	44	
A48 IL_l/ML N 122	M	91.62	94.90	94.11	93.50	93.63	87.60	1 vs. 5 2 vs. 5, 3 vs. 5 4 vs. 5
	S.D.	7.05	5.08	6.14	3.03	7.85	6.75	
		122	32	22	4	15	49	
A49 Arch width M_1–M_1 upper N 127	M	44.34	43.27	44.35	43.24	44.31	43.87	1 vs. 5
	S.D.	2.41	2.11	2.11	2.20	2.72	2.54	
		127	32	23	5	15	52	
A50 Arch width M_1–M_1 lower N 127	M	40.82	40.58	40.56	40.38	40.88	41.11	
	S.D.	2.40	2.14	2.21	2.10	2.80	2.59	
		127	32	23	5	15	52	
A51 Arch width 04–04 upper N 115	M	33.97	34.88	34.00	33.12	34.49	33.60	
	S.D.	2.66	2.91	2.27	2.20	2.79	2.77	
		115	21	25	11	13	45	
A52 Arch width 04–04 lower N 89	M	29.87	30.48	29.40	30.30	29.94	29.63	
	S.D.	1.94	2.15	1.93	1.57	1.99	1.92	
		89	18	15	9	11	36	
A53 Arch length upper N 114	M	34.90	35.27	34.28	32.60	34.78	34.07	1 vs. 3 4 vs. 3 5 vs. 3
	S.D.	2.46	2.22	2.91	0.28	2.36	2.37	
		114	32	22	2	13	45	

Table 8 *Mean (M) and standard deviation* (S D) *of year of birth for the children in the five groups*
Significant differences ($P<0.01$) between the groups are listed in the last column

Variable		Total	Group 1 Controls No adenoids $n=37$	2 Controls Small adenoids $n=33$	3 Controls Large adenoids $n=11$	4 Adenoidectomy Otit. med $n=21$	5 Adenoidectomy Nasal obstr $n=60$	Significant differences $P<0.01$
A02								
Age (year of birth)	M	58.60	58.10	58 77	59 72	58 45	58.65	3 vs. 1 3 vs. 5
$N=162$	S.D	1 70	1.59	1.89	1.27	2.14	1.56	
	S.E.	0 13	0.22	0.33	0.38	0 48	0.20	

The significant differences between groups 5 and 1 in respect of large tonsils (A17) and swollen nasal mucosa (A18) are no doubt connected with the high incidence of obstructed nose breathing (A13–14) and recurrent infections in the ear nose and throat (A06) noted for group 5

A particularly noteworthy significant difference is that between groups 5 and 1 concerning variable A09 Number of siblings with ear nose and throat diseases

The mean ages of the five groups, expressed by year of birth are shown in Table 8

The children in control group 3 i e. children with large radiographic size of adenoids but no clinical discomfort, have a significantly younger mean age than those in groups 1 and 5 i.e controls without adenoids and adenoidectomy children with obstructed nose breathing respectively

Summary

The results presented in Table 7 appear to fully justify the present classification of the children into five groups There is a large number of significant intergroup differences particularly between the control groups (1 2 and 3) and the adenoidectomy groups (4 and 5) Control group 3 which comprises children with large radiographic size of adenoids on the posterior wall of nasopharynx but no clinical discomfort occupies an intermediate position between the other two control groups and the adenoidectomy groups in the case of the variables connected with mode of breathing. With the exception of age which is lower for group 3 than group 1 no significant differences have been found between the three control groups. Between the adenoidectomy groups (4 and 5) on the other hand there are significant differences for mouth open in sleep open or closed mouth, nasal obstruction (left and right) mouth breathing and the variable for size of tonsils. The children who underwent adenoidectomy for nasal obstruction included a higher proportion of mouth breathers and large tonsils than those who underwent adenoidectomy on account of recurrent otitis media. This supports *obstructed nose breathing* as the otologist s indication for adenoidectomy

Dentition variables

Data concerning dentition variables are presented in Table 9 (for definitions see Table 1)

As will be seen from the last column of Table 9 there are several significant differences between the group means In the case of several dentition variables the largest differences are mostly between the means for groups 1 and 5 This is particularly noteworthy since as will be seen from Table 7 these two groups also differ most in respect of mode of breathing (A04 05 15) and nasal obstruction (A13 14 16)

Furthermore the means for several denti

Table 9 *Mean* (*M*) *and standard deviation* (S.D.) *of dentition variables for the children in the five groups*

The number of children (*n*) is indicated for variables with a drop-out of more than 10 %, i.e. if N < 145. Significant differences ($P < 0.01$) are listed in the last column (the group with the higher mean has been compared with the group or groups with lower means)

Variable		Total	Group 1 Controls No adenoids = 37	Group 2 Controls Small adenoids = 33	Group 3 Controls Large adenoids = 11	Group 4 Adenoidectomy Oth. med. = 21	Group 5 Adenoidectomy Nasal obstr. = 60	Significant differences $P < 0.01$
A42 ss & sm projected on OL *N* 158	*M*	−0.59	−0.50	−0.01	0.16	−0.87	−0.99	
	S.D.	2.66	2.86	2.13	1.83	2.54	2.94	
A43 Freeway space preop. *N* 90	*M*	8.71	6.74	9.96	3.57	9.07	10.03	
	S.D.	14.05	10.81	16.64	1.07	13.90	15.82	
		90	21	16	6	10	37	
A44 OL/ML *N* 158	*M*	15.84	14.97	15.41	15.10	14.58	17.15	5 vs. 4
	S.D.	3.90	3.94	3.68	2.82	3.13	4.10	
A45 OL/NSL *N* 158	*M*	19.32	17.64	19.94	18.20	18.76	20.39	5 vs. 1, 2 vs. 1
	S.D.	3.66	3.03	3.22	3.07	3.62	3.96	
A46 IL$_s$/NSL *N* 113	*M*	102.70	106.70	101.84	101.63	103.57	100.07	1 vs. 5
	S.D.	6.89	4.07	7.23	7.71	7.37	7.01	
		113	31	19	4	15	44	
A47 IL$_s$/IL$_i$ *N* 113	*M*	129.65	125.39	126.85	128.38	128.23	134.47	5 vs. 1, 5 vs. 2
	S.D.	9.23	3.95	6.60	9.78	9.44	10.12	
		113	31	19	4	15	44	
A48 IL$_i$/ML *N* 122	*M*	91.62	94.90	94.11	93.50	93.63	87.60	1 vs. 5, 2 vs. 5, 3 vs. 5, 4 vs. 5
	S.D.	7.05	5.08	6.14	3.03	7.85	6.75	
		122	32	22	4	15	49	
A49 Arch width M_1–M_1 upper *N* 127	*M*	44.34	45.27	44.35	43.24	44.31	43.87	1 vs. 5
	S.D.	2.41	2.11	2.11	2.20	2.72	2.54	
		127	32	23	5	15	52	
A50 Arch width M_1–M_1 lower *N* 127	*M*	40.82	40.58	40.56	40.38	40.88	41.11	
	S.D.	2.40	2.14	2.21	[illegible]	2.80	2.59	
		127	32	23	5	15	52	
A51 Arch width 04–04 upper *N* 115	*M*	33.97	34.88	34.00	33.12	34.49	33.60	
	S.D.	2.66	2.91	2.27	2.20	2.79	2.77	
		115	21	23	11	13	45	
A52 Arch width 04–04 lower *N* 89	*M*	29.87	30.48	29.40	30.30	29.94	29.63	
	S.D.	1.94	2.15	1.93	1.52	1.99	1.92	
		89	18	15	9	11	36	
A53 Arch length upper *N* 114	*M*	34.50	35.27	34.28	32.60	34.78	34.07	1 vs. 3, 4 vs. 3, 5 vs. 3
	S.D.	2.46	2.22	[illegible]	0.28	2.36	2.37	
		114	32	22	2	13	45	

Table 9 *Cont*

Variable		Total	Group 1 Controls No adenoids $n=37$	2 Controls Small adenoids $n=33$	3 Controls Large adenoids $n=11$	4 Adenoidectomy Otit med. $n=21$	5 Adenoidectomy Nasal obstr $n=60$	Significant differences $P<0.01$
A54 Arch length lower								
$N=122$	M	30.81	31 63	30.73	3[illegible]58	31.56	29.88	1 vs. 5
	S.D	[illegible]56	1 46	2.16	7.28	[illegible]37	2.29	
	n	1[illegible]2	32	[illegible]	5	15	48	
A55 Overjet								
$N=135$	M	3 19	3.4	3.14	2.61	3.36	3.07	
	S.D	1 69	1 98	1 48	1.21	1 89	1 6[illegible]	
	n	135	34	29	7	18	47	
A56 Overbite								
$N=131$	M	2.19	2.71	2.30	0.48	2.58	1 79	1 vs. 3 2 vs. 3, 4 vs. 3
	S.D	1 76	1 75	1.58	1 45	1.23	1 93	
	n	131	34	29	6	18	44	
A57 Sagittal relation M M right								
$N=126$	M	1 00	0.98	0 63	−0.58	0 73	1 46	
	S.D	2.61	[illegible]38	1 98	3.43	[illegible]75	2.84	
	n	126	32	23	6	15	50	
A58 Sagittal relation M_1–M left								
$N=1$[illegible]5	M	1 04	0 68	1.28	−0.73	0.28	1.58	
	S D	2.53	[illegible]45	2.47	3.87	3 10	[illegible]16	
	n	125	32	[illegible]3	6	14	50	
A59 Crossbite								
$N=160$	M	1 11	1 03	1 06	1 18	1.05	1[illegible]1	5 vs. 1
	S.D	0.3	0.16	0.24	0.41	0.22	0.41	
A60 Height of palatal vault at M M								
$N=117$	M	13.04	13.54	11 79	13 05	12.89	13.32	
	S.D	2.59	2.00	3.12	0.35	2.41	[illegible]67	
	n	117	3	2[illegible]	2	14	47	
A61 Space difference of upper arch								
$N=159$	M	1 87	[illegible]41	1 73	0.82	[illegible]86	1 43	
	S.D	5.02	4.58	4.50	5.33	5.32	5 44	
A62 Space difference of lower arch								
$N=159$	M	−0.86	−0.53	−1.[illegible]3	0.15	−0.90	−1.05	
	S.D	4.29	4 79	3.97	3.81	4 75	4 15	
A63 Lower arch width M_1–M_1 100 / Upper arch width M–M								
$N=123$	M	91 95	89 66	91 41	93 60	91 43	93.64	3 vs. 1 5 vs. 1
	S.D	4 92	[illegible]44	4 32	[illegible]88	4 13	6.03	
	n	123	3	22	5	14	50	
A64 Lower arch width 04–04 100 / Upper arch width 04–04								
$N=85$	M	88.29	87.33	85 71	91.22	88.00	89 06	3 vs.
	S.D	5 10	5.27	3 17	3.77	3 98	5.8[illegible]	
	n	85	15	14	9	11	36	
A65 Upper arch length 100 / Upper ar[illegible]idth M M								
$N=112$	M	77 87	78.06	77 90	72.00	78.[illegible]3	77 86	1 vs. 3 2 vs. 3 4 vs. 3 5 vs. 3
	S D	5 64	4 75	7.20	1 41	4 02	5 96	
	n	11	32	21	2	13	44	
A66 Height of palatal [illegible]ault 100 / Upper arch width M M								
N 114	M	29 8[illegible]	[illegible]9 97	[illegible]7 80	28.50	29.[illegible]1	30.83	
	S.D	5 15	4 71	4.23	0.71	6.28	5 42	
	n	114	32	20	2	14	46	

tion variables in group 3 differ significantly from the corresponding means in groups 1 and 5 Here, however it should be remembered that the children in group 3 have a significantly younger mean age than those in groups 1 and 5 (cf. Table 8)

Group 5 differs significantly from the other groups in respect of the mean for variable A48, i.e. inclination of the lower incisors in relation to the mandibular line Group 5 has the lowest mean, indicating that on the average the lower incisors are more retroclined in these children.

In the case of variable A47 i.e. the mutual inclination of the lower and upper incisors, group 5 has a significantly higher mean than groups 1 and 2. This is partly a consequence of the circumstance that group 5 also has a significantly lower mean than group 1 for variable A46, i e inclination of the upper incisors in relation to the nasion-sella line Thus the upper incisors are more retroclined on the average in the children belonging to group 5

Group 5 has a significantly higher mean than group 1 for variable A45 i e angle between occlusal and nasion-sella lines Group 2 also differs significantly from group 1 in this respect.

Group 5 has a significantly higher mean than group 4 for variable A44 i.e. angle between occlusal and mandibular lines. The means for variables A49 Upper arch width between first molars, and A54 Lower arch length, are significantly smaller for group 5 than for group 1 On the other hand, group 5 has significantly higher means than group 1 for variables A59 Crossbite, and A63 Index for lower and upper arch widths between first molars Group 3 also has a significantly higher mean than group 1 in the case of variable A63

In the case of the related variables A53 Length of upper arch, and A65 Index for length and breadth of upper arch, group 3 has significantly lower means than groups 1 4 and 5

Group 3 also has a significantly lower mean than groups 1 2 and 4 for variable A56, Over bite.

Summary

The results in Table 9 show that the children in adenoidectomy group 5 tend to have retroclined upper and lower incisors, a narrow upper arch, a short lower arch, a high incidence of crossbite and wide angles between the occlusal line on the one hand and the nasion-sella and mandibular lines on the other Otherwise the significant differences in Table 9 refer to comparisons between the controls in group 3 and other groups On the average the children in group 3 appear to have a short upper arch and a small overbite It should be noted, however that the children in group 3 have a significantly younger mean age than the controls in group 1 and the children in adenoidectomy group 5

Adenoid variables

Data concerning adenoid variables are presented in Table 10 (for definitions see Table 1) Variables connected with the postoperative size of adenoids (A21 27 28 30 31 33 34 36, 37 39 and 41) were not of course relevant in the case of the controls (groups 1 2 and 3)

There is a large number of significant differences between the group means. In the case of several adenoid variables the largest differences are mostly between group 1 and the other groups. This is in accordance with the group definitions. The large significant differences between control groups 1 and 2 on the one hand and the adenoidectomy groups 4 and 5 on the other for size of adenoids (variables A20, 6, 9 32, 35 38 and 40) were also expected and agree with the definitions of controls and subjects. On the other hand, the high means for these variables in group 3 were unexpected since these children had been included as controls because the clinical assessment showed them to be free of discomfort. These means in group 3 are in fact significantly different from those in group 1 Concerning these variables, moreover it is only for A38 that the means in groups 3 and 5 are significantly different, while no significant differences were

Table 10 *Mean (M) and standard deviation* (S D) *of adenoid variables for the children in the five groups*

The number of children (*n*) is indicated for variables with a drop-out of more than 10 % i. e. if $N < 145$. Significant differences ($P < 0.01$) are listed in the last column (the group with the higher mean has been compared with the group or groups with lower means)

Variable		Total	Group: 1 Controls No adenoids $n = 37$	2 Controls Small adenoids $n = 33$	3 Controls Large adenoids $n = 11$	4 Adenoidectomy Otit. med. $n = 21$	5 Adenoidectomy Nasal obstr $n = 60$	Significant differences $P < 0.01$
A20 Adenoid size before adenoidectomy $N = 16$[illegible]	*M*	2.77	1.00	2.27	4.00	3.00	3 82	2 vs. 1 3 vs. 1 4 vs. 1 5 vs. 1 3 vs. 2, 4 vs. 2, 5 vs. 2, 5 vs. 4
	S.D	1.25	0	0.45	0	0 71	0.68	
A21 Adenoid size after adenoid ectomy $N = 81$	*M*	1.54				1 48	1.58	
	S.D	0.67				0 75	0.65	
	n	81				21	60	
Indication for adenoidectomy								
A22 Obstructed nose breathing $N = 160$	*M*	1.38	1 00	1 00	1 00	1.05	1.98	5 vs. 4
	S.D	0.49	0	0	0	0.22	0.13	
A23 Recurrent infection $N = 159$	*M*	1.25	1.00	1.00	1.00	1.33	1.54	
	S.D	0 44	0	0	0	0 48	0.50	
A[illegible]4 Recurrent otitis media $N = 160$	*M*	1 19	1.00	1.00	1 00	1 76	1.25	4 vs. 5
	S.D	0 40	0	0	0	0.44	0.44	
A25 Allergy $N = 160$	*M*	1.01	1.00	1.00	1.00	1.05	1.00	
	S.D	0.08	0	0	0	0.22	0	
A26 ad –ba preop. $N = 162$	*M*	28.08	2[illegible].80	25 75	30.[illegible]5	29 74	31 64	vs. 1 3 vs. 1 4 vs. 1 5 vs. 1 3 vs. 2, 4 vs. 2, 5 vs. 2
	S.D	5 67	3.30	5.34	3.56	5 13	4 41	
A27 ad –ba postop. $N = 81$	*M*	20.53				20.43	20.56	
	S.D	4 65				3 45	5 01	
	n	81				21	60	
A28 ad –ba difference $N = 81$	*M*	10.71				9.56	11 10	
	S.D	4 76				4 49	4.83	
	n	81				21	60	
A29 ad_1–ho preop $N = 162$	*M*	16.37	13 00	15 12	16.29	17 46	18.25	[illegible]. 1 3 vs. 1 4 [illegible]. 1 5 vs. 1 4 vs. 2, 5 vs. 2
	S.D	3.46	2.20	2.56	[illegible].82	2.82	[illegible].80	
A30 ad_1–ho postop. $N = 81$	*M*	12.91				1[illegible].65	12.99	
	S.D	3 16				3.33	3 12	
	n	81				21	60	
A31 ad_1–ho difference $N = 81$	*M*	5 64				5.20	5 79	
	S D	2.85				[illegible].60	2.9[illegible]	
	n	81				21	60	

Table 10. *Cont*

Variable		Total	Group 1 Controls No adenoids *n* = 37	Group 2 Controls Small adenoids 33	Group 3 Controls Large adenoids 11	Group 4 Adenoidectomy Otit. med. *n* = 21	Group 5 Adenoidectomy Nasal obstr *n* = 60	Significant differences $P < 0.01$
A32 Adenoid area 100 / pm–ho–ba–pm preop. *N* 162	*M*	84.34	73.64	81.82	87.18	86.15	91 19	2 vs. 1 3 vs. 1 4 vs. 1 5 vs. 1 5 vs. 2
	S.D	9 79	7.26	7.23	6.44	10.45	5.23	
A33 Adenoid area 100 / pm–ho–ba–pm postop. *N* 81	*M*	69 75				69.28	69.91	
	S.D	10.88				10.49	11.09	
		81				21	60	
A34 Adenoid area 100 / pm–ho–ba–pm difference *N* 81	*M*	20.70				18.84	21.33	
	S D	9.58				8.62	9.87	
		81				21	60	
A35 Adenoid area 100 / pm–ho–ba–ho'–pm preop. *N* 162	*M*	64.52	53 87	60.33	70.16	67.51	71.30	2 vs. 1 3 vs. 1 4 vs. 1 5 vs. 1 3 vs. 2, 4 vs. 2, 5 vs. 2
	S.D	10.54	6.77	7.28	5.91	8.26	8.99	
A36 Adenoid area 100 / pm–ho–ba–ho'–pm postop. *N* 81	*M*	50.14				49.88	50.23	
	S.D.	8.47				7.02	8.96	
		81				21	60	
A37 Adenoid area 100 / pm–ho–ba–ho –pm difference *N* 81	*M*	20 34				18.51	20.96	
	S.D	8.76				8.25	8.91	
		81				21	60	
A38 ad_1–ho 100 / pm–ho preop. *N* 162	*M*	57.96	44.84	53.58	60.00	60.67	67 15	2 vs. 1 3 vs. 1 4 vs. 1 5 vs. 1 4 vs. 2, 5 vs. 2, 5 vs. 3
	S.D.	12.28	7 44	7 71	7.35	9.83	9 78	
A39 ad_1–ho 100 / pm–ho postop. *N* 81	*M*	45.85				43.95	46.49	
	S.D	10.91				11.52	10.71	
		81				21	60	
A40 ad_1–ba 100 / pm–ba preop. *N* 162	*M*	64.95	51.08	59.00	69.64	67.81	74.97	2 vs. 1 3 vs. 1 4 vs. 1 5 vs. 1 3 vs. 2, 4 vs. 2, 5 vs. 2
	S.D	13.58	7.22	11 10	8.07	10.84	10.24	
A41 ad_1–ba 100 / pm–ba postop. *N* 81	*M*	48.01				46.75	48.44	
	S.D	10.27				9.02	10.70	
		81				21	60	

obtained between groups 3 and 4 Size of adenoids measured radiographically is thus the same on the average for the children in groups 3 and 4 and considerably larger than for those in group 1

A significant difference of particular interest is that between groups 4 and 5 for variable A20 i e. size of adenoids in relation to the nasopharynx. The children who were adenoid ectomized for obstructed nose breathing thus appear to have a larger mean size of adenoids than those who underwent the operation on account of recurrent otitis media

The significant differences between groups 4 and 5 for variables A22 and A24 i e obstructed nose breathing and recurrent otitis media respectively as indications for adenoid ectomy are to be regarded as a consequence of the definitions of these groups.

Summary

As shown by Table 10 the means for size of adenoids display a large number of significant intergroup differences. The differences between the control groups (1 2 and 3) were expected and agree with the definitions of these groups The existence of group 3 with its high means is unexpected however as the clinical assess ment of these children showed them to be free of discomfort. The significant differences in means for size of adenoids between the adenoi dectomy groups (4 and 5) is particularly interesting. The children adenoidectomized for obstructed nose breathing appear to have had larger adenoids on the average than those who underwent the operation on account of recur rent otitis media

Airflow variables

Data concerning airflow variables are presented in Table 11 (for definitions see Table 1) It should be noted that variables A67–72 con cern nasal airflow at the first examination i e immediately before adenoidectomy in the case of groups 4 and 5 while variables A73–78 refer to the examination one month later i e. 1 month after adenoidectomy in the case of groups 4 and 5 Furthermore variables A67–69 and A73–75 concern nasal airflow before nose drops, whereas A70–72 and A76–78 concern nasal airflow after nose drops

Variables A67 A70 A73 and A76 express nasal airflow measured at a differential pressure of 10 mm H_2O while the corresponding measurements at a differential pressure of 15 mm H_2O are expressed by A68, A71 A74 and A77 and those at 20 mm H_2O by A69 A72 A75 and A78

As will be seen from Table 11 nasal airflow measurements were obtained for between 8 and 10 children in group 3 which is considerably fewer than in any of the other groups.

The very low means for nasal airflow in group 3 (see Table 11) are particularly note worthy According to the clinical assessment, adenoidectomy was not indicated in these children who were therefore accepted as controls The radiographic assessment however showed that group 3 had large adenoids in relation to the bony nasopharynx (cf variables A20 A32 and A35 in Table 10) The consistently low means for nasal airflow in group 3 appear to support the radiographic assessment of the size of adenoids in these children.

Groups 1 and 2 were also classified according to the radiographic assessment of size of adenoids whereas groups 4 and 5 were obtained from the indication for adenoidectomy recurrent otitis media and obstructed nose breathing respectively

There is a large number of significant inter group differences. As far as the first examination is concerned, these differences mostly apply to mean airflow before nose drops (A67 68) between groups 1 and 2 on the one hand and groups 3 and 5 on the other Furthermore the means for variables A67–69 display significant differences between groups 4 and 3 After nose drops at the first examination variables A70–71 (corresponding to A67–68 before nose drops) show significant differences only between group 1 and groups 2 3 and 5 Variable A72 i e airflow measured at 20 mm

Table 11. *Mean (M) and standard deviation (S.D.) of airflow variables for the children in the five groups*

Significant differences ($P < 0.01$) are listed in the last column (the group with the higher mean has been compared with the group or groups with lower means)

Variable		Total	Group 1 Controls No adenoids 37	Group 2 Controls Small adenoids 33	Group 3 Controls Large adenoids 11	Group 4 Adenoidectomy Otit. med. –21	Group 5 Adenoidectomy Nasal obstr –60	Significant differences $P < 0.01$
A67 Preop. airflow before nose drops	*M*	17.77	21.10	18.82	13.35	18.99	15.29	1 vs. 3, 1 vs. 5, 2 vs. 3, 2 vs. 5, 4 vs. 3
N 138	S.D.	5.30	4.83	5.12	3.70	5.17	4.31	
		138	35	30	10	16	47	
A68 Preop. airflow before nose drops	*M*	22.48	26.29	23.71	16.45	24.65	19.30	1 vs. 3, 1 vs. 5, 2 vs. 3, 2 vs. 5, 4 vs. 3
N 130	S.D.	6.47	5.56	6.28	3.89	7.12	5.10	
		130	35	29	10	13	43	
A69 Preop. airflow before nose drops	*M*	25.38	30.61	25.60	18.65	27.68	21.89	1 vs. 2, 1 vs. 3, 1 vs. 5, 2 vs. 3, 4 vs. 3
N 124	S.D.	7.37	6.55	7.10	4.38	8.26	5.16	
		124	33	26	10	14	41	
A70 Preop. airflow after nose drops	*M*	25.63	30.82	25.78	21.39	25.37	22.59	1 vs. 2, 1 vs. 3, 1 vs. 5
N 138	S.D.	7.18	7.43	5.51	6.13	7.02	5.96	
		138	36	29	9	15	49	
A71 Preop. airflow after nose drops	*M*	32.08	38.46	31.68	27.06	33.14	28.29	1 vs. 2, 1 vs. 3, 1 vs. 5
N 130	S.D.	9.02	8.54	7.29	8.20	9.28	7.86	
		130	35	28	9	11	47	
A72 Preop. airflow after nose drops	*M*	33.31	40.59	36.33	28.56	36.21	32.32	1 vs. 3, 1 vs. 5
N 122	S.D.	8.87	6.92	8.14	8.01	9.60	8.62	
		122	28	27	8	14	45	
A73 Postop. airflow before nose drops	*M*	19.03	20.75	18.34	14.38	20.26	18.54	1 vs. 3, 4 vs. 3
N 135	S.D.	5.55	4.96	4.94	4.21	5.50	6.07	
		135	34	29	8	17	47	
A74 Postop. airflow before nose drops	*M*	23.50	25.62	23.29	18.13	24.50	22.67	1 vs. 3, 4 vs. 3
N 130	S.D.	6.74	5.79	6.57	4.42	6.57	7.39	
		130	33	28	8	16	45	
A75 Postop. airflow before nose drops	*M*	26.78	30.15	26.62	21.00	28.00	25.11	1 vs. 3, 1 vs. 5, 4 vs. 3
N 128	S.D.	7.33	6.09	7.96	4.77	7.14	7.25	
		128	31	29	8	16	44	
A76 Postop. airflow after nose drops	*M*	28.02	32.86	26.57	20.89	26.97	27.16	1 vs. 2, 1 vs. 3, 1 vs. 5, 5 vs. 3
N 144	S.D.	7.76	7.67	5.77	6.45	8.21	7.33	
		144	35	28	9	17	55	
A77 Postop. airflow after nose drops	*M*	33.39	38.10	3[illegible].79	25.06	32.75	32.55	1 vs. 3, 1 vs. 3, 2 vs. 3, 5 vs. 3
N 136	S.D.	8.36	8.33	7.14	7.31	10.14	7.80	
		136	31	28	9	16	52	
A78 Postop. airflow after nose drops	*M*	37.43	42.71	37.80	28.11	33.50	37.03	1 vs. 3, 1 vs. 4, 1 vs. 5, 2 vs. 3, 5 vs. 3
N 128	S.D.	9.[illegible]3	8.57	8.28	7.22	8.74	8.85	
		128	28	28	9	14	49	

H_2O after nose drops (corresponding to A69 before nose drops) shows significant differences only between group 1 and groups 3 and 5

None of the means in group 4 differ from those in groups 1 and 2 for variables A67–72 i.e. airflow at the first examination before as well as after nose drops This is remarkable considering the differences found in size of adenoids between group 4 and groups 1 and 2 (cf variables A20 A32 and A35 in Table 10)

Concerning the second examination, i.e. 1 month after adenoidectomy in the case of groups 4 and 5 the significant differences for airflow before nose drops (A73–75) mostly involve groups 1 and 4 on the one hand and group 3 on the other These differences were also found at the first examination (variables A67–69)

The significant differences between groups 1 and 5 before adenoidectomy and before nose drops (A67–69) were repeated before nose drops after adenoidectomy only in the case of airflow measured at a differential pressure of 20 mm H_2O (A75) Airflow after nose drops at the second examination (1 month after adenoidectomy for groups 4 and 5 variables A76–78) is significantly different not only between group 1 and groups 3 and 5 as it was at the first examination (A70–72) but also between group 5 and group 3

It appears from Table 11 that nasal airflow is increased after adenoidectomy However 1 month after the operation the mean values for the adenoidectomy children had not reached the same level as those for group 1 i e children with no clinical or radiographic signs of adenoids on the posterior wall of the nasopharynx

Group 3 which comprises children with no clinical indications for adenoidectomy but large adenoids according to the radiographic assessment, displays relatively similar means for airflow at the first and second examinations (compare A67–72 with A73–78)

Since the largest size of adenoids at the first examination is found in groups 3 and 5 (cf A20 A32 and A35 in Table 10) these groups can be expected to display similar means for airflow at the first examination. This is confirmed in Table 11 by the good agreement between groups 3 and 5 in mean airflow at the first examination after nose drops (A70–72) At the second examination, i e. 1 month after adenoidectomy in group 5 (A76–78), mean airflow after nose drops is considerably higher in group 5 than in group 3

A picture of the percentage distribution of nasal airflow is provided by Fig. 23 *a–h*, in which the controls in group 1 are compared with the adenoidectomy children (groups 4 and 5) It will be seen that before adenoidectomy groups 4 and 5 have a considerably lower airflow than group 1 and that the differences are not as pronounced after the operation. These results agree with the findings in Table 11

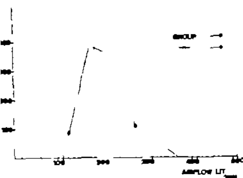
Concerning airflow before adenoidectomy however it will be seen from Fig. 23 *a–h* that there is a certain amount of overlapping. Thus, Fig. 23 *a* shows that 51% of the children in group 1 have an airflow of more than 20 lit/min but only 7% of group 5 and that only 9 of group 1 had an airflow of less than 15 lit/min compared with 48% of group 5 Overlapping is least pronounced in Figs. 23 *a* and 23 *b* After adenoidectomy the degree of overlapping is notably greater and there are no significant differences between the means.

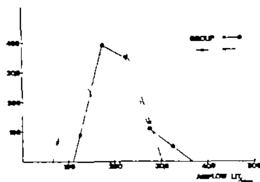
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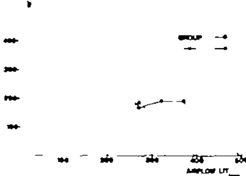
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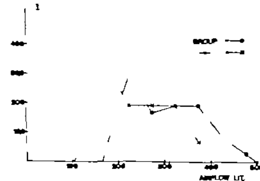
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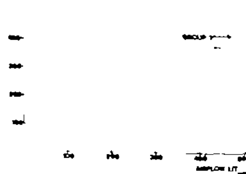
Fig 23 Airflow diagrams, (*a* and *e*) before nose drops and before adenoidectomy (*b* and *f*) after nose drops before adenoidectomy (*c* and *g*) before nose drops after adenoidectomy (*d* and *h*) after nose drops after adenoidectomy *a b c* and *d* compare the children in groups 1 and 5, *e f g* and *h* compare those in groups 1 and 4. The plots indicate the percentage of children in the various airflow classes and thus give the distribution. Each class has a range of 5 l t/min and the plots have been located in the centre of the class.

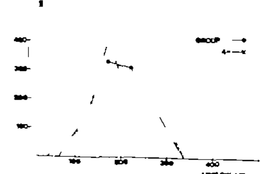

PREOP AIRFLOW BEFORE NOSE DROPS
GROUP
AIRFLOW LIT

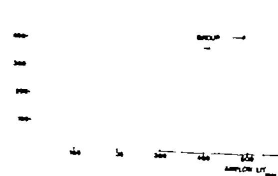

PREOP AIRFLOW BEFORE NOSE DROPS
GROUP
AIRFLOW LIT

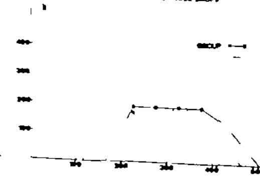

PREOP AIRFLOW AFTER NOSE DROPS
GROUP
AIRFLOW LIT


PREOP AIRFLOW AFTER NOSE DROPS
GROUP
AIRFLOW LIT


POSTOP AIRFLOW BEFORE NOSE DROPS
GROUP
AIRFLOW LIT


POSTOP AIRFLOW BEFORE NOSE DROPS
GROUP
AIRFLOW LIT


POSTOP AIRFLOW AFTER NOSE DROPS
GROUP
AIRFLOW LIT


POSTOP AIRFLOW AFTER NOSE DROPS
GROUP
AIRFLOW LIT

H_2O after nose drops (corresponding to A69 before nose drops) shows significant differences only between group 1 and groups 3 and 5

None of the means in group 4 differ from those in groups 1 and 2 for variables A67–72, i.e. airflow at the first examination before as well as after nose drops. This is remarkable considering the differences found in size of adenoids between group 4 and groups 1 and 2 (cf variables A20 A32 and A35 in Table 10)

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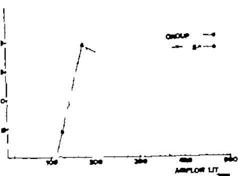
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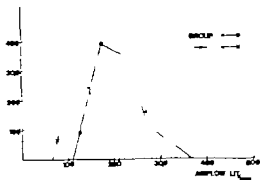
Summary

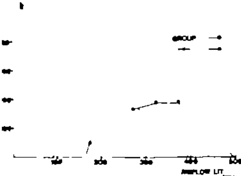
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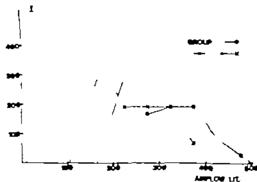
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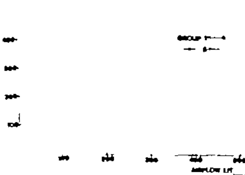
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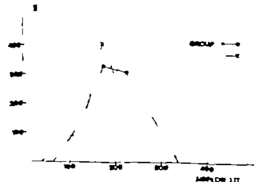

PREOP AIRFLOW BEFORE NOSE DROPS
GROUP
100
200
300
400
500
AIRFLOW LIT

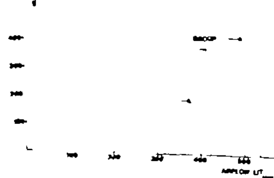

PREOP AIRFLOW BEFORE NOSE DROPS
GROUP
AIRFLOW LIT

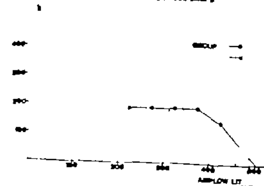

PREOP AIRFLOW AFTER NOSE DROPS
GROUP
AIRFLOW LIT


PREOP AIRFLOW AFTER NOSE DROPS
GROUP
AIRFLOW LIT


POSTOP AIRFLOW BEFORE NOSE DROPS
GROUP
AIRFLOW LIT


POSTOP AIRFLOW BEFORE NOSE DROPS
GROUP
AIRFLOW LIT


POSTOP AIRFLOW AFTER NOSE DROPS
GROUP
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Summary

From Table 11 it can be seen that nasal air flow at a differential pressure of 10 mm H_2O varies partly on account of enlarged adenoids The table shows that airflow is increased after adenoidectomy One month after the operation however the mean airflow in the adenoid-

Fig. 23 Airflow diagrams, (*a* and *e*) before nose drops and before adenoidectomy (*b* and *f*) after nose drops before adenoidectomy (*c* and *g*) before nose drops after adenoidectomy (*d* and *h*) after nose drops after adenoidectomy *a b c* and *d* compare the children in groups 1 and 5 *e f g* and *h* compare those in groups 1 and 4 The plots indicate the percentage of children in the various airflow classes and thus give the distribution Each class has a range of 5 lit/min and the plots have been located in the centre of the class.

Table 12. *Cont*

Variable		Total	Group: 1 Controls No adenoids = 37	2 Controls Small adenoids = 33	3 Controls Large adenoids = 11	4 Adenoidectomy Otit. med. = 21	5 Adenoidectomy Nasal obstr = 60	Significant differences $P<0.01$
A95 pm–ba *N* 162	*M* S.D	35.57 2.77	36.08 3.02	34.66 2.36	33.18 2.09	35.84 2.23	36.09 2.81	1 vs. 3 4 vs. 3 5 vs. 3
A96 Height of upper lip *N* 162	*M* S.D	22.51 2.22	22.03 2.29	22.24 1.79	21.25 1.37	22.78 1.97	23.00 2.44	5 vs. 3
A97 Height of lower lip *N* 162	*M* S.D	38.32 3.71	37.82 3.54	37.51 4.62	35.77 3.98	38.00 2.64	39.64 3.13	5 vs. 3
A98 fmt–fmt *N* 128	*M* S.D	95.22 3.56 128	96.68 4.40 30	94.26 3.28 28	92.70 3.52 10	95.35 3.23 13	95.35 2.83 47	1 vs. 3
A99 lo–lo *N* 161	*M* S.D.	87.13 3.08	87.76 3.45	86.84 3.04	85.17 2.77	86.66 3.47	87.43 2.65	
A100 bch–bch *N* 152	*M* S.D.	26.01 2.28	26.83 2.18	25.25 2.23	25.21 2.00	26.22 1.94	26.00 2.38	1 vs. 2
A101 bch–bch bo ⊥ pm–ba pm–ba ∫ *N* 152	*M* S.D	8850.02 1533.10	9448.57 1689.84	8436.48 1189.27	7890.63 1740.69	8906.80 1463.34	8854.61 1475.95	1 vs. 2
A102 s–n–ss *N* 162	*M* S.D	81.09 3.64	82.55 3.66	80.50 2.70	81.68 4.40	81.93 4.72	80.11 3.24	1 vs. 2, 1 vs. 5
A103 s–n–sm *N* 162	*M* S.D	77.00 3.24	78.78 3.38	75.95 2.17	77.45 2.89	77.83 3.74	76.10 3.05	1 vs. 2, 1 vs. 5
A104 s–n–ss 82° *N* 162	*M* S.D	1.46 0.50	1.62 0.49	1.30 0.47	1.55 0.52	1.62 0.50	1.37 0.49	1 vs. 2
A105 ss–n–sm *N* 162	*M* S.D.	4.09 2.31	3.77 2.36	4.55 1.93	4.23 2.75	4.07 2.86	4.01 [illegible]	
A106 ML/NSL *N* 162	*M* S.D	35.34 5.20	32.62 4.29	35.74 4.05	33.32 4.06	33.43 4.45	37.83 5.58	2 vs. 1 5 vs. 1 5 vs. 3 5 vs. 1
A107 ML/NL *N* 162	*M* S.D	28.86 5.24	26.54 3.56	28.67 4.86	26.95 3.72	27.50 3.31	31.23 6.16	5 vs. 1 5 vs. 3 5 vs. 4
A108 NL/NSL *N* 162	*M* S.D	6.51 2.90	6.07 2.78	7.13 3.06	6.41 1.96	6.00 2.44	6.64 3.17	
A109 ba–s–pm *N* 16[illegible]	*M* S.D	62.69 5.26	63.47 4.57	63.80 4.32	66.36 [illegible]	62.71 5.81	60.90 5.74	2 vs. 5 3 vs. 5
A110 n–s–ba *N* 16[illegible]	*M* S.D.	132.21 4.57	132.99 4.71	133.14 4.30	134.36 4.77	130.74 4.60	131.59 4.45	

Table 12. *Mean (M) and standard deviation (S.D.) of skeleton and lip variables for the children in the five groups*

The number of children (*n*) is indicated for variables with a drop-out of more than 10% i. e. if $N < 145$. Significant differences ($P < 0.01$) are listed in the last column (the group with the higher mean has been compared with the group or groups with lower means)

Variable		Total	Group: 1 Controls No adenoids n = 37	2 Controls Small adenoids n = 33	3 Controls Large adenoids n = 11	4 Adenoidectomy Otit. med n = 21	5 Adenoidectomy Nasal obstr n = 60	Significant differences $P < 0.01$
A80 Face width N = 162	M	103.61	105.19	102.62	101.85	103.28	103.63	
	S.D	3.93	4.49	3.79	3.87	2.67	3.80	
A81 Face height N = 162	M	94.40	94.17	92.71	89.50	93.50	96.68	5 vs. 2, 5 vs. 3, 5 vs. 4
	S.D	5.44	5.72	5.20	5.20	3.94	4.97	
A82 Nose width over alae nasi N = 162	M	28.98	29.26	28.65	27.64	29.49	29.05	1 vs. 3, 4 vs. 3
	S.D	1.97	1.62	2.03	1.64	1.49	2.25	
A83 Nose width above alae nasi N = 162	M	20.40	20.34	19.90	19.78	21.01	20.62	4 vs. 3
	S.D	1.63	1.10	1.65	0.95	1.53	1.91	
A84 Height of upper lip N = 162	M	19.41	19.51	19.11	18.71	19.69	19.54	
	S.D	1.64	1.85	1.62	1.27	1.16	1.71	
A85 n–s N = 162	M	66.33	66.83	66.40	65.04	66.25	66.26	
	S.D	2.97	2.99	2.69	2.43	3.76	[illegible].91	
A86 s–ba N = 162	M	40.74	41.25	39.97	39.10	41.11	41.03	
	S.D	3.01	3.46	2.32	2.84	2.05	3.26	
A87 n–ba N = 162	M	98.53	99.61	98.15	96.49	98.50	98.45	
	S.D	4.48	4.53	3.29	4.06	4.83	4.91	
A88 n–gn N = 162	M	104.40	104.20	102.48	99.11	102.92	107.08	5 vs. 2, 5 vs. 3, 5 vs. 4
	S.D	6.00	6.16	5.69	6.16	4.80	5.29	
A89 n–sp N = 162	M	46.34	46.57	45.99	43.53	45.74	47.1	1 vs. 3, 5 vs. 3
	S.D	2.95	3.18	2.94	3.05	2.80	2.53	
A90 sp–gn N = 162	M	58.37	58.71	56.49	55.58	57.18	60.13	5 vs. [illegible], 5 vs. 3, 5 vs. 4
	S.D	5.10	7.31	4.03	4.15	2.88	4.10	
A91 ss–pm N = 162	M	44.48	45.42	44.21	43.15	44.47	44.30	
	S.D	2.39	2.75	1.67	3.35	1.88	2.31	
A92 pm–ba N = 162	M	43.36	44.72	43.21	43.65	43.87	42.39	1 vs. 5
	S.D	3.29	3.25	2.09	3.08	3.65	3.51	
A93 ho ⊥ pm–ba N = 162	M	15.60	15.57	15.46	14.19	15.46	16.01	5 vs. 3
	S.D	1.81	1.82	1.47	1.96	2.12	1.73	
A94 s–pm N = 162	M	42.73	43.72	41.98	40.36	43.08	4[illegible].84	1 vs. 3, 4 vs. 3, 5 vs. 3
	S.D	2.83	2.85	2.64	[illegible].31	2.45	[illegible].86	

Table 1. *Cont*

Variable		Total	Group: 1 Controls No adenoids = 37	2 Controls Small adenoids = 33	3 Controls Large adenoids = 11	4 Adenoid-ectomy Oth. med. = 21	5 Adenoid-ectomy Nasal obstr n = 60	Significant differences $P < 0.01$
A123 ho pm-ba pm-ba ∤ *N* 162	*M* S.D	338.33 44.35	348.37 47.65	335.54 32.50	311.32 61.21	337.37 44.48	338.98 43.57	
A124 s-n-ba N 162	*M* S.D.	63.19 3.58	65.03 3.39	63.95 3.43	65.00 3.56	64.14 4.14	62.31 3.18	1 vs. 5
A125 pm-ho-ba N 162	*M* S.D	107.98 8.39	110.20 6.98	108.42 5.96	113.95 5.89	109.07 9.47	104.89 9.33	1 vs. 5 3 vs. 5
A126 n-ho N 162	*M* S.D	73.56 3.43	74.42 3.62	73.27 2.42	71.64 2.84	73.87 4.52	73.43 3.37	
A127 ho N 162	*M* S.D	19.99 1.82	20.54 1.77	19.29 1.90	18.94 0.95	20.44 1.44	20.08 1.89	1 vs. 2, 1 vs. 3 4 vs. 3, 5 vs. 3
A128 Body height N 108	*M* S.D	129.32 4.57 108	131.78 4.71 32	126.70 4.30 22	120.79 4.77 7	133.57 4.60 9	129.34 4.57 38	1 vs. 3, 5 vs. 3

ectomy children had not reached the level recorded in children with no clinical or radiographic signs of adenoids. The number of significant intergroup differences in respect of mean airflow values seems to fully justify the division of the material into these groups.

Skeleton and lip variables

The results for skeleton and lip variables are shown in Table 1 (for definitions see Table 1)

There are several significant differences between the means for the various groups.

Total face height (A81 A88) is significantly larger in group 5 than in groups ., 3 and 4

Anterior upper face height (A89) is significantly larger in groups 1 and 5 than in group 3 Anterior lower face height (A90) is significantly larger in group 5 than in groups 2, 3 and 4

Nose width (*A82*) is significantly larger in groups 1 and 4 than in group 3

The sagittal depth of the bony nasopharynx (*A92*) is significantly smaller in group 5 than in group 1 The volume of the bony nasopharynx (A101) is significantly *greater in group* 1 than in group 2. The height of the bony nasopharynx (A93) *is significantly greater in* group 5 than in group 3

Posterior upper face height (A94 A95) is significantly smaller in group 3 than in groups 1 4 and 5

Face width (A98) is significantly greater in group 1 than in group 3

The posterior choanal aperture (A100) is significantly wider in group 1 than in group 2 Th. angles s-n-ss and s-n-sm (A102 and A103 respectively) are significantly wider in group 1 than in groups 2 and 5

The angle between the mandibular line and the nasion-sella line (A106) is significantly

Table 12. *Cont*

Variable		Total	Group: 1 Controls No adenoids $n=37$	2 Controls Small adenoids $n=33$	3 Controls Large adenoids $n=11$	4 Adenoidectomy Otit med $n=21$	5 Adenoidectomy Nasal obstr $n=60$	Significant differences $P<0.01$
A111 Face width 100 / Face height $N=162$	*M*	109.96	111 89	110 85	113 82	110 48	107 40	1 vs. 5 2 vs. 5, 3 vs. 5
	S.D	5.85	5 75	5 39	6.13	5.22	5 43	
A112 fmt–fmt × 100 / n–gn $N=127$	*M*	91 47	92.20	9[illegible].07	94 10	92.46	89 78	
	S.D	4 69	4 90	4 98	5.02	4.52	3.92	
	n	127	30	28	10	13	46	
A113 lo–lo × 100 / n–gn $N=160$	*M*	83.53	84.32	84.82	86.27	84.20	81.58	1 vs. 5 2 vs. 5
	S D	4 80	4 16	5.32	5 76	4 78	4 09	
A114 n–s 100 / n–gn $N=162$	*M*	63 74	64 32	64 97	65 73	64.90	61 93	1 vs. 5 2 vs. 5, 3 vs. 5 4 vs. 5
	S D	3.82	4 10	3 69	2.76	3 10	3 47	
A115 ss pm 100 / n–gn $N=162$	*M*	42.72	43 70	43.24	43.55	43.38	41 45	1 vs. 5 2 vs. 5 4 vs. 5
	S.D	2.71	2.99	[illegible].70	2.77	2.52	2.59	
A116 n–sp 100 / n–gn $N=162$	*M*	44.38	44 70	44.85	44 00	44.52	43.95	
	S D	1 80	1 66	1 99	1 95	1 44	1.80	
A117 ss pm 100 / n–sp $N=162$	*M*	96.24	97 76	96.42	99 27	97 48	94.22	
	S.D	6 76	7 37	6.01	8.26	7.05	5 98	
A118 ho–ba 100 / pm–ba $N=162$	*M*	58.14	56.27	58.12	57 36	57 43	59 70	5 vs. 1
	S D	5 02	4 03	4 69	3 70	6.38	5 08	
A119 s–ba 100 / n–s $N=162$	*M*	61 46	61.89	60.27	60 09	62.14	61 85	
	S.D	4 63	5 06	3 99	4 48	4 15	4.83	
A120 pm–ba 100 / ho + pm–ba $N=16$[illegible]	*M*	278 01	289 62	273.06	311 45	275 86	268 20	3 vs. 5
	S.D	49 82	41 95	52.10	36.77	77 02	39 75	
A121 pm–ho $N=162$	*M*	28.17	29 05	27 51	27.05	28 87	27 95	
	S.D	2.68	2.30	4.02	2.20	2.84	1 71	
A122 ba–ho $N=162$	*M*	25 03	25 15	24 46	25 00	25.04	25.28	
	S.D	2.96	2.51	4.29	2.61	2.12	2.69	

Table 12. *Cont*

Variable		Total	Group: 1 Controls No adenoids 37	2 Controls Small adenoids = 33	3 Controls Large adenoids = 11	4 Adenoidectomy Oth. med. = 21	5 Adenoidectomy Nasal obstr. = 60	Significant differences $P < 0.01$
A123 ho pm-ba pm-ba) *N* 162	*M*	338.33	348.37	335.54	311.32	337.57	338.98	
	S.D	44.35	47.65	32.50	61.21	44.48	43.57	
A124 s-n-ba *N* 162	*M*	63.19	65.03	63.95	65.00	64.14	62.31	1 vs. 5
	S.D	3.58	3.39	3.43	3.56	4.14	3.18	
A125 pm-ho-ba *N* 162	*M*	107.98	110.20	108.42	113.95	109.07	104.89	1 vs. 5 3 vs. 5
	S.D	8.39	6.98	5.96	5.89	9.47	9.33	
A126 n-ho *N* 162	*M*	73.56	74.42	73.27	71.64	73.87	73.43	
	S.D	3.43	3.62	2.42	2.84	4.52	3.37	
A127 ho *N* 162	*M*	19.99	20.54	19.29	18.94	20.44	20.08	1 vs. 2, 1 vs. 3 4 vs. 3 5 vs. 3
	S.D.	1.82	1.77	1.90	0.95	1.44	1.89	
A128 Body height *N* 108	*M*	129.32	131.78	126.70	120.79	133.57	129.34	1 vs. 3, 5 vs. 3
	S.D	4.57	4.71	4.30	4.77	4.60	4.57	
		108	32	22	7	9	38	

ectomy children had not reached the level recorded in children with no clinical or radiographic signs of adenoids. The number of significant intergroup differences in respect of mean airflow values seems to fully justify the division of the material into these groups.

Skeleton and lip variables

The results for skeleton and lip variables are shown in Table 12 (for definitions see Table 1).

There are several significant differences between the means for the various groups.

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Nose width (A82) is significantly larger in groups 1 and 4 than in group 3.

The sagittal depth of the bony nasopharynx (A92) is significantly smaller in group 5 than in group 1. The volume of the bony nasopharynx (A101) is significantly greater in group 1 than in group 2. The height of the bony nasopharynx (A93) is significantly greater in group 5 than in group 3.

Posterior upper face height (A94 A95) is significantly smaller in group 3 than in groups 1, 4 and 5.

Face width (A98) is significantly greater in group 1 than in group 3.

The posterior choanal aperture (A100) is significantly wider in group 1 than in group.

The angles s–n–ss and s–n–sm (A102 and A103 respectively) are significantly wider in group 1 than in groups 2 and 5.

The angle between the mandibular line and the nasion-sella line (A106) is significantly

Table 12, *Cont*

Variable		Total	Group: 1 Controls No adenoids $n=37$	2 Controls Small adenoids $n=33$	3 Controls Large adenoids $n=11$	4 Adenoid-ectomy Otit. med. $n=21$	5 Adenoid ectomy Nasal obstr $n=60$	Significant differences $P<0.01$
A111 Face width 100 / Face height $N=162$	M	109 96	111 89	110.85	113.82	110 48	107 40	1 vs. 5, 2 vs. 5, 3 vs. 5
	S.D	5 85	5 75	5.39	6.13	5.22	5.43	
A112 fmt–fmt 100 / n–gn $N=127$	M	91 47	92.20	92.07	94 10	92.46	89 78	
	S.D	4 69	4 90	4 98	5.02	4.52	3.92	
	n	127	30	28	10	13	46	
A113 lo–lo 100 / n–gn $N=160$	M	83.53	84.32	84 82	86.27	84.20	81.58	1 vs. 5 2 vs. 5
	S.D	4 80	4 16	5 32	5 76	4 78	4 09	
A114 n–s 100 / n–gn $N=162$	M	63 74	64.32	64 97	65 73	64 90	61 93	1 vs. 5, 2 vs. 5, 3 vs. 5 4 vs. 5
	S D	3.82	4 10	3 69	2.76	3 10	3 47	
A115 ss pm 100 / n–gn $N=162$	M	4[illegible]72	43.70	43.24	43.55	43.38	41 45	1 vs. 5 2 vs. 5 4 vs. 5
	S D	2.71	2.99	2.70	[illegible]77	2.52	2.59	
A116 n–sp 100 / n–gn $N=162$	M	44.38	44 70	44.85	44.00	44.52	43 95	
	S.D	1 80	1 66	1 99	1 95	1 44	1.80	
A117 ss pm 100 / n–sp $N=162$	M	96.24	97 76	96.42	99.27	97 48	94.22	
	S.D	6.76	7 37	6.01	8[illegible]6	7 05	5 98	
A118 ho–ba 100 / pm–ba $N=162$	M	58.14	56.27	58.12	57 36	57 43	59 70	5 vs. 1
	S.D	5 02	4 03	4 69	3 70	6.38	5 08	
A119 s–ba 100 / n–s $N=162$	M	61 46	61 89	60.27	60 09	62.14	61 85	
	S.D	4 63	5 06	3.99	4 48	4 15	4 83	
A120 pm–ba 100 / ho ⊥ pm–ba $N=162$	M	278.01	289 62	273 06	311 45	[illegible]75 86	[illegible]68.20	3 vs. 5
	S.D	49 82	41 95	52.10	36.77	77 02	39 75	
A121 pm–ho $N=162$	M	28.17	29 05	[illegible]7.51	27 05	28.87	[illegible]7 95	
	S.D	2.68	2.30	4 02	2.20	2.84	1 71	
A122 ba–ho $N=162$	M	[illegible]5.03	[illegible]5 15	[illegible]4 46	25.00	25.04	25.28	
	S.D	[illegible]96	[illegible]51	4.29	2.61	2.12	[illegible]69	

Table 14 Correlations between all pairs of variables for anamnesis and clinical status

The table only shows correlation coefficients that are significant at the 1% level ($r \geq 0.20$, the sign of neglected, i.e. $\leq$ 0.20 or $\geq$ 0.20)

Variable	A	02	03	04	05	06	07	08	09	10	13	14	15	16	17	18	19
Age	02																
Sex	03																
Mode of breathing	04																
Mouth in sleep	05			.65													
Infec. in ear n. & throat	06			.60	.54												
Allergy	07																
Prev adenoidectomy	08			.26	.25	.23											
Siblings ear n. & throat dis.	09				.23												
Prolonged finger-sucker	10																
Obstruc. nose breathing, left	13			41	.53	47											
Obstruc. nose breathing, right	14			45	.52	.51		.29			.88						
Mouth breathing	15			70	77	.64					.66	.65					
Enlarged adenoid	16			71	69	.64					.56	.53	77				
Large tonsils	17				.26	.26		.33					.26				
Swollen nasal mucosa	18										.24	.21					
Septum deviation	19						.20										

bles. This is because variables A129–131 were measured only (*a*) in the controls in group 1 whose size of adenoids (A32) was less than the mean for this group (73 64%) and (*b*) in the children in group 5 i.e. adenoidectomy for obstructed nose breathing, whose value for the same variable was greater than the mean for this group (91 19%)

Significant differences between the means for groups 1 and 5 are shown for the shortest distance between the tongue and pterygomaxillare (A129) as well as for the shortest distance between the tongue and the midpoint of the soft palate (A131)

Summary

Table 13 indicates that the children in this study who underwent adenoidectomy for obstructed nose breathing appear to have held the tongue in a lower position than the children whose nasal passages were unobstructed.

SIMPLE CORRELATION ANALYSES

Correlations between variables concerning anamnesis and clinical status

Simple correlations between all pairs of anamnesis and clinical status variables except A11 and A12 are presented in Table 14 Variable A11 Previous orthodontic therapy is not included—either here or subsequently—because it was found that only three children in the entire material had previously received such therapy Variable A12, Open or closed mouth, was excluded as it correlates strongly with A15 Mouth breathing. For definitions of the variables see Table 1

As will be seen, a large number of correlations in Table 14 are significant at the 1% level, i.e. the correlation coefficient $|r| \geq 0.20$

Furthermore, all correlations between variables A04–06, A13–15 are significant at the 0 1% level, i.e. $|r| \geq 0\ 40$ With the exception of A06, these variables have to do with the mode of breathing and the presence of nasal obstruction. The significant correlations between these variables and A16 Enlarged adenoids, support the current opinion that size of adenoids strongly influences the mode of breathing and contributes to recurrent infections in the ear nose and throat.

Previous adenoidectomy (A08) is significantly correlated to large tonsils (A17), certain variables concerning mode of breathing (A04–05) and recurrent infections in the ear nose and throat (A06).

The correlations for A17 Large tonsils, show that this finding is more frequent in children

Table 13 *Mean (M) and standard deviation* (S D) *of variables connected with tongue position for the children in groups 1 and 5*

Significant differences ($P < 0.01$) between the means for the two groups are listed in the last column

Variable		Total	Group 1 Controls No adenoids $n = 37$	2 Controls Small adenoids $n = 33$	3 Controls Large adenoids $n = 11$	4 Adenoidectomy Otit med. $n = 21$	5 Adenoidectomy Nasal obstr $n = 60$	Significant differences $P < 0.01$
A129								
pm–t preop, rest position	M	10.46	8 47				11 97	5 vs. 1
$N = 51$	S D	3 16	2.28				2.91	
	n	51	22				29	
A130								
ba–t preop rest position	M	39 90	38.73				40.79	
$N = 51$	S D	3 87	2.89				4.31	
	n	51	22				29	
A131								
$\frac{pm-v}{2}$ –t preop rest position	M	2.91	1.86				3.74	5 vs. 1
$N = 50$	S D	2.20	1.56				2.23	
	n	50	22				28	

greater in group 5 compared with groups 1 3 and 4 as well as in group 2 compared with group 1

The angle between the mandibular line and the nasal line (A107) is significantly greater in group 5 than in groups 1 3 and 4

The angle between pterygomaxillare (pm) and the midpoint of sella turcica (s) and basion (ba) (A109) is significantly smaller in group 5 than in groups 2 and 3

Body height (A128) is significantly smaller in group 3 than in groups 1 and 5

The index for face width/face height (A111) is significantly lower in group 5 than in groups 1 2 and 3

The index for depth of cranial base/face height (A114) is significantly lower in group 5 than in groups 1 2 3 and 4

The index for face depth/face height (A115) is significantly lower in group 5 than in groups 1 2 and 4 Height of upper lip (A96) and height of lower lip (A97) are both significantly larger in group 5 than in group 3

The majority of the significant intergroup differences in Table 12 refer to the children in group 5 on the one hand and those in one or several of groups 1–4 on the other

Summary

Table 12 indicates that, in relation to one or several of the other groups, the children who underwent adenoidectomy for obstructed nose breathing (group 5) have on the average a large face height, short nasopharynx in the sagittal plane a great tendency to small values for the angles s–n–ss and s–n–sm a great angle between the mandibular and the nasion-sella lines as well as the nasal line, low indexes for face width/height face depth/height and depth of cranial base/face height as well as great height of upper and lower lips The children in group 5 thus appear to have a particular facial morphology

Variables for tongue position

The results for variables that express the position of the tongue in relation to the hard and soft palates are given in Table 13

Considerably fewer children are represented in Table 13 than in the other groups of varia-

Table 14 *Correlations between all pairs of variables for anamnesis and clinical status*

The table only shows correlation coefficients that are significant at the 1% level (≥0.20 the sign of neglected, i.e. ≤ 0.20 or ≥0.20)

Variable	A	02	03	04	05	06	07	08	09	10	13	14	15	16	17	18	19
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Siblings' ear n. & throat dis.	09				.33												
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Obstruc. nose breathing, right	14			45	.52	.51		.29			.88						
Mouth breathing	15			70	77	.64					66	.65					
Enlarged adenoid	16			71	69	.64					.56	.53	77				
Large tonsils	17				.26	.26		.33					.26				
Swollen nasal mucosa	18										.24	.21					
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bles. This is because variables A129–131 were measured only (*a*) in the controls in group 1 whose size of adenoids (A32) was less than the mean for this group (73.64%), and (*b*) in the children in group 5 i.e. adenoidectomy for obstructed nose breathing, whose value for the same variable was greater than the mean for this group (91 19%)

Significant differences between the means for groups 1 and 5 are shown for the shortest distance between the tongue and pterygomaxillare (A129) as well as for the shortest distance between the tongue and the midpoint of the soft palate (A131)

Summary

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Furthermore, all correlations between variables A04–06 A13–15 are significant at the 0 1% level, i e $|r| \geq 0\ 40$ With the exception of A06 these variables have to do with the mode of breathing and the presence of nasal obstruction. The significant correlations between these variables and A16 Enlarged adenoids, support the current opinion that size of adenoids strongly influences the mode of breathing and contributes to recurrent infections in the ear nose and throat.

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Significant differences ($P < 0.01$) between the means for the two groups are listed in the last column

Variable		Total	Group 1 Controls No adenoids $n = 37$	2 Controls Small adenoids $n = 33$	3 Controls Large adenoids $n = 11$	4 Adenoidectomy Otit med $n = 21$	5 Adenoidectomy Nasal obstr $n = 60$	Significant differences $P < 0.01$
A129 pm–t preop. rest position $N = 51$	M	10.46	8.47				11 97	5 vs. 1
	S D	3 16	2.28				2.91	
	n	51	22				29	
A130 ba–t_1 preop rest position $N = 51$	M	39 90	38.73				40.79	
	S.D	3 87	2.89				4 31	
	n	51	22				29	
A131 $\frac{pm-v}{2}$ – t preop rest position $N = 50$	M	2.91	1 86				3 74	5 vs. 1
	S.D	2.20	1.56				2.23	
	n	50	22				28	

greater in group 5 compared with groups 1 3 and 4 as well as in group 2 compared with group 1

The angle between the mandibular line and the nasal line (A107) is significantly greater in group 5 than in groups 1 3 and 4

The angle between pterygomaxillare (pm) and the midpoint of sella turcica (s) and basion (ba) (A109) is significantly smaller in group 5 than in groups 2 and 3

Body height (A128) is significantly smaller in group 3 than in groups 1 and 5

The index for face width/face height (A111) is significantly lower in group 5 than in groups 1 2 and 3

The index for depth of cranial base/face height (A114) is significantly lower in group 5 than in groups 1 2, 3 and 4

The index for face depth/face height (A115) is significantly lower in group 5 than in groups 1 2 and 4 Height of upper lip (A96) and height of lower lip (A97) are both significantly larger in group 5 than in group 3

The majority of the significant intergroup differences in Table 12 refer to the children in group 5 on the one hand and those in one or several of groups 1–4 on the other

Summary

Table 12 indicates that, in relation to one or several of the other groups, the children who underwent adenoidectomy for obstructed nose breathing (group 5) have on the average a large face height, short nasopharynx in the sagittal plane a great tendency to small values for the angles s–n–ss and s–n–sm a great angle between the mandibular and the nasion-sella lines as well as the nasal line low indexes for face width/height face depth/height and depth of cranial base/face height as well as great height of upper and lower lips. The children in group 5 thus appear to have a particular facial morphology

Variables for tongue position

The results for variables that express the position of the tongue in relation to the hard and soft palates are given in Table 13

Considerably fewer children are represented in Table 13 than in the other groups of varia-

Table 16. *Correlations between variables for anamnesis and clinical status on the one hand and adenoid variables on the other*

The table only shows correlation coefficients that are significant at the 1 % level (≥0.20)

A20 Ad. size before adenoidectomy
A21 Ad. size after adenoidectomy
A22–A25 Indication for adenoidectomy: A22 obstr. nose breathing; A23 recurrent infection; A24 recurrent otitis media; A25 allergy

A26 ad_1–ba preop.
A27 ad_1–ba postop.
A28 ad_1–ba difference
A29 ad_4–ho preop.
A30 ad_4–ho postop.
A31 ad_4–ho difference

A32 $\frac{\text{Ad. area} \quad 100}{\text{pm–ho–ba–pm}}$ preop.
A33 $\frac{\text{Ad. area} \quad 100}{\text{pm–ho–ba–pm}}$ postop.
A37 $\frac{\text{Ad. area} \quad 100}{\text{pm–ho–ba–ho'–pm}}$ difference

Variable	A	20	21	22	23	24	25	26	27	28	29	30	31	32	33	37
Age	02	.23	.33		.22									.26		
Sex	03															
Mode of breathing	04	49	.31	.39	45	.36		.39	.36	44	.53	40		42		–.31
Mouth in sleep	05	.57		.68	45	.31		44			49			41		
Infec. in ear n. & throat	06	.50		.56	63	.30		.32			41			.37		
Allergy	07															
Prev adenoidectomy	08										..1					
Siblings ear n. & throat dis.	09	.25				.26										
Prolonged finger-sucker	10															
Obstruc. nose breathing, left	13	.60		.62	.35	.25		41			48		40	48		43
Obstruc. nose breathing, right	14	.55		.58	.34	.30		.33			43			42		.33
Mouth breathing	15	66		75	.54	.29		.31			.57			.55		
Enlarged adenoids	16	71		73	.54	48		.57	.31		64			.60		
Large tonsils	17			.22	.22											
Swollen nasal mucosa	18				.22											
Septum deviation	19															

index for width of lower and upper arches (A63) and an index for height of palatal vault and upper arch width (A66) variables for the inclination of the upper and lower incisors (A46–48) and variables for the angles between the occlusal line and the mandibular and nasion-sella lines (A44–45)

These correlations indicate that children who breath through the mouth tend to have a narrow upper arch, crossbite or a tendency to crossbite, short lower jaw retroclination of upper and lower incisors, and large angles between the occlusal line and the mandibular and nasion-sella lines.

There is also a significant correlation between prolonged finger suckers (A10) and small overbite (A56)

Large tonsils (A17) is significantly correlated with the dentition variables that express the vertical relationship between the upper and lower arches (A44 and A56) The presence of large tonsils appears to be associated with a small overbite.

Year of birth (A02) shows significant correlations with several dentition variables, i.e. width of upper arch between the first deciduous molars (A52), overbite (A56) height of palatal vault (A60) space difference of upper arch (A61) and the index for height of palatal vault and upper arch width (A66) Correlations between age and dentition variables are to be expected in particular when the latter represent measurements of size

Summary

The significant correlations shown in Table 15 between variables for anamnesis and clinical status on the one hand and dentition variables on the other confirm the suspicion that there is a relationship between mode of breathing and characteristics of the dentition. They indicate that children who breath through the mouth have a narrow upper arch, crossbite or a tendency to crossbite, short lower arch, retroclination of upper and lower incisors, and

Table 15 *Correlations between variables for anamnesis and clinical status on the one hand and dentition variables on the other*

The table only shows correlation coefficients that are significant at the 1 level ($r \geq 0.20$)

A02 Age
A03 Sex
A04 Mode of breathing
A05 Mouth in sleep
A06 Infec. in ear n. & throat
A07 Allergy
A08 Prev adenoidectomy
A09 Siblings ear n. & throat dis.
A10 Prolonged finger-sucker
A13 Obstruc. nose breathing, left
A14 Obstruc. nose breathing, right
A15 Mouth breathing
A16 Enlarged adenoids
A17 Large tonsils
A18 Swollen nasal mucosa
A19 Septum deviation

Variable	A	02	03	04	05	06	07	08	09	10	13	14	15	16	17	18	19
ss & sm proj on OL	42																
Freeway space preop	43			.30				.37									
OL/ML	44				.23								.25		–.1		
OL/NSL	45				.20			.20			.22	.22	.25				
IL_s/NSL	46				–.27						–.26		–.23	–.25			
IL_s/IL_i	47				.31						.25		34	.35			
IL_i/ML	48			–.26	.31	–.23					–.31	–.31	– 46	41			
Arch width M_1–M upper	49											.24	–.27				
Arch width M_1–M lower	50																
Arch width 04–04 lower	52	–.34															
Arch length, upper	53																
Arch length, lower	54				–.28						–.27	–.26	.33				
Overjet	55																
Overbite	56	– 40						–.24		–.24					.25		
Sagittal rel. M M right	57																
Sagittal rel. M_1–M left	58					.23											
Crossbite	59											.20					
H of pal vault at M_1–M	60	–.59															
Space diff of upper arch	61	.26															
Space diff of lower arch	6.																
Lower arch width M –M_1 100 / Upper arch width M M	63			.24							.25	.28	.31	.30			
Lower arch width 04–04 100 / Upper arch width 04–04	64												.28				
Upper arch length 100 / Upper arch width M M	65																
H of pal vault M_1 M_1 100 / Upper arch width M –M	66	– 62			.30								.25				

who suffer from recurrent infections in the ear nose and throat as well as in mouth breathers

Table 14 also indicates that children who sleep with the mouth open (A05) frequently have siblings who suffer from ear nose and throat diseases (A09)

Summary

The correlations shown in Table 14 are dominated by the positive relationships between mouth breathing on the one hand and variables for the nasal airway on the other The correlation between mouth breathing and enlarged adenoids is particularly marked The presence of large tonsils, on the other hand appears to be of less importance for mode of breathing.

Variables for anamnesis and clinical status correlated with dentition variables

Correlations between variables for anamnesis and clinical status on the one hand and dentition variables on the other are shown in Table 15 Variable A51 Arch width 04–04 upper is not included as it correlates strongly with A49 Arch width M_1–M_1 upper

There are a great many significant correlations ($P < 0.01$) The majority of substantial correlations refer to breathing variables (A04–05 A13–16) on the one hand and on the other variables that express width of upper arch at first molars (A49 and A66) and length of lower arch (A54) variables representing an

Table 16. *Correlations between variables for anamnesis and clinical status on the one hand and adenoid variables on the other*

The table only shows correlation coefficients that are significant at the 1 % level ($r \geq 0.20$)

A20 Ad. size before adenoidectomy
A21 Ad. size after adenoidectomy
A22–A25 Indication for adenoidectomy: obstr. nose breathing (A22), recurrent infection (A23), recurrent otitis media (A24), allergy (A25)
A26 ad_1–ba preop.
A27 ad_1–ba postop.
A28 ad_1–ba difference
A29 ad_2–ho preop.
A30 ad_2–ho postop.
A31 ad_2–ho difference
A32 $\frac{\text{Ad. area} \quad 100}{\text{pm–ho–ba–pm}}$ preop.
A33 $\frac{\text{Ad. area} \quad 100}{\text{pm–ho–ba–pm}}$ postop
A37 $\frac{\text{Ad. area} \quad 100}{\text{pm–ho–ba–ho'–pm}}$ difference

Variable	A	20	21	22	23	24	25	26	27	28	29	30	31	32	33	37
Age	02	.23	.33		.22									.26		
Sex	03															
Mode of breathing	04	49	.31	.59	.45	.36		.39	.36	44	.53	40		42		.31
Mouth in sleep	05	.57		.68	.45	.31		43			49			41		
Infec. in ear n. & throat	06	.50		.56	.63	.30		.32			41			.37		
Allergy	07															
Prev adenoidectomy	08										.21					
Siblings ear n. & throat dis.	09	.25				.26										
Prolonged finger-sucker	10															
Obstruc. nose breathing, left	13	.60		.62	.35	.23		41			48		40	48		43
Obstruc. nose breathing, right	14	.55		.58	.34	.30		.33			43			42		.33
Mouth breathing	15	.66		75	.54	.29		.51			.57			.55		
Enlarged adenoids	16	71		73	.34	48		.57	.31		64			.60		
Large tonsils	17			.22	.22											
Swollen nasal mucosa	18				.22											
Septum deviation	19															

index for width of lower and upper arches (A63) and an index for height of palatal vault and upper arch width (A66) variables for the inclination of the upper and lower incisors (A46–48) and variables for the angles between the occlusal line and the mandibular and nasion-sella lines (A44–45)

These correlations indicate that children who breath through the mouth tend to have a narrow upper arch, crossbite or a tendency to crossbite, short lower jaw retroclination of upper and lower incisors, and large angles between the occlusal line and the mandibular and nasion-sella lines.

There is also a significant correlation between prolonged finger suckers (A10) and small overbite (A56)

Large tonsils (A17) is significantly correlated with the dentition variables that express the vertical relationship between the upper and lower arches (A44 and A56). The presence of large tonsils appears to be associated with a small overbite

Year of birth (A02) shows significant correlations with several dentition variables, i.e. width of upper arch between the first deciduous molars (A52), overbite (A56), height of palatal vault (A60), space difference of upper arch (A61), and the index for height of palatal vault and upper arch width (A66) Correlations between age and dentition variables are to be expected in particular when the latter represent measurements of size.

Summary

The significant correlations shown in Table 15 between variables for anamnesis and clinical status on the one hand and dentition variables on the other confirm the suspicion that there is a relationship between mode of breathing and characteristics of the dentition. They indicate that children who breath through the mouth have a narrow upper arch, crossbite or a tendency to crossbite, short lower arch, retroclination of upper and lower incisors, and

Table 15 *Correlations between variables for anamnesis and clinical status on the one hand and dentition variables on the other*

The table only shows correlation coefficients that are significant at the 1% level ($r \geq 0.20$)

A02 Age
A03 Sex
A04 Mode of breathing
A05 Mouth in sleep
A06 Infec. in ear n. & throat
A07 Allergy
A08 Prev adenoidectomy
A09 Siblings ear n. & throat dis.
A10 Prolonged finger-sucker
A13 Obstruc. nose breathing, left
A14 Obstruc. nose breathing, right
A15 Mouth breathing
A16 Enlarged adenoids
A17 Large tonsils
A18 Swollen nasal mucosa
A19 Septum deviation

Variable	A	02	03	04	05	06	07	08	09	10	13	14	15	16	17	18	19
ss & sm proj on OL	42																
Freeway space preop.	43			.30				.37									
OL/ML	44				.23								..5		.21		
OL/NSL	45				.20			.20			.22	.22	.25				
IL_s/NSL	46				.27						–.26		–.23	.25			
IL_s/IL_i	47				.31						.25		34	.35			
IL_i/ML	48			–..6	–.31	–.23					–.31	–.31	–46	41			
Arch width M M upper	49											.24	–.27				
Arch width M –M_1 lower	50																
Arch width 04-04 lower	52	–.34															
Arch length, upper	53																
Arch length, lower	54				–.28						–.27	–.26	–.33				
Overjet	55																
Overbite	56	–40						–.24		–.24					–.25		
Sagittal rel. M –M right	57																
Sagittal rel. M_1–M left	58					.23											
Crossbite	59											.20					
H of pal vault at M_1–M	60	–.59															
Space diff of upper arch	61	.26															
Space diff of lower arch	62																
Lower arch width M_1 M_1 100 / Upper arch width M M	63			.24							.25	.28	.31	.30			
Lower arch width 04-04 100 / Upper arch width 04-04	64												.28				
Upper arch length 100 / Upper arch width M M	65																
H of pal vault M_1 M_1 100 / Upper arch width M –M	66	–62			30								..5				

who suffer from recurrent infections in the ear nose and throat as well as in mouth breathers

Table 14 also indicates that children who sleep with the mouth open (A05) frequently have siblings who suffer from ear nose and throat diseases (A09)

Summary

The correlations shown in Table 14 are dominated by the positive relationships between mouth breathing on the one hand and variables for the nasal airway on the other The correlation between mouth breathing and enlarged adenoids is particularly marked. The presence of large tonsils, on the other hand appears to be of less importance for mode of breathing.

Variables for anamnesis and clinical status correlated with dentition variables

Correlations between variables for anamnesis and clinical status on the one hand and dentition variables on the other are shown in Table 15 Variable *A51 Arch width 04–04* upper is not included as it correlates strongly with A49 Arch width M_1–M_1 upper

There are a great many significant correlations ($P < 0.01$) The majority of substantial correlations refer to breathing variables (A04–05 A13–16) on the one hand and on the other variables that express width of upper arch at first molars (A49 and A66) and length of lower arch (A54) variables representing an

Table 17 *Correlations between variables for anamnesis and clinical status on the one hand and airflow variables on the other*

The table only shows correlation coefficients that are significant at the 1% level (≥0.20)

Variable	A	Preop. airflow before nose drops 67	Preop. airflow after nose drops 70	Postop. airflow before nose drops 73	Postop. airflow after nose drops 76
Age	02		−.26		−.22
Sex	03				
Mode of breathing	04				
Mouth in sleep	05	−.24	−.29		
Infec. in ear n. & throat	06				
Allergy	07				
Prev adenoidectomy	08				
Siblings' ear n. & throat dis.	09	−.30	−.24		
Prolonged finger-sucker	10				
Obstruc. nose breathing, left	13	45	−.34		
Obstruc. nose breathing, right	14	−.37	−.30		
Mouth breathing	15	−.30	−.32		
Enlarged adenoids	16	−.29	−.34		
Large tonsils	17				
Swollen nasal mucosa	18	−.26		−.25	−.22
Septum deviation	19				

as half the number of children had undergone adenoidectomy in the interval and this presumably improved their nasal airflow

There are significant negative correlations between the number of siblings with ear nose and throat diseases (A09) and airflow variables A67 and A70 This is probably explained by the positive relationship between variable A09 and size of adenoids (A20) reported in Table 16

The age variable (A07) also displays significant correlations with airflow variables A70 and A76. Since age is expressed by year of birth, low ages are represented by high values and consequently a positive relationship between airflow and increasing age is denoted with a minus sign.

Summary

The significant negative correlations in Table 17 between anamnesis and clinical status variables expressing nasal obstruction on the one hand and nasal airflow on the other indicate that there is good agreement between the subjective and objective methods of registration employed in this investigation.

Variables for anamnesis and clinical status correlated with skeleton and lip variables

Significant correlations between anamnesis and clinical status variables on the one hand and skeleton and lip variables on the other are presented in Table 18 Variables A12, A81 A98 A112 and A126 are not included as they correlate very strongly with variables A15 A88 A99 A113 and A87 respectively

Many of the correlations between these variables are significant ($P < 0.01$)

The age variable (A02) is significantly correlated to the majority of skeleton and lip variables, the strongest relationship ($r = 0.86$) being with body height (A128) It is particularly interesting that there is no significant correlation between age and the sagittal depth

large angles between the occlusal line on the one hand and the mandibular and nasion-sella lines on the other In addition the presence of large tonsils appears to be associated with a small overbite.

Variables for anamnesis and clinical status correlated with adenoid variables

Significant correlations between variables for anamnesis and clinical status on the one hand and adenoid variables on the other are shown in Table 16 Variables A34–36 and A38–41 are not included since they correlate strongly with A33 A26 A27 A29 A30 A26 and A27 respectively

There are several relatively strong correlations between the variables for mode of breathing (A04–05 A15) and those for preoperative size of adenoids in relation to the nasopharynx (A20 A26 A29 and A32) This strongly suggests that mouth breathing is a consequence of enlarged adenoids

It was to be expected that the anamnesis and clinical status variables which express mode of breathing (A04–05 A15) or the causes and presence of nasal obstruction (A06 A13–14 A16 and A18) would be significantly correlated with the variables for indications for adenoidectomy i.e obstructed nose breathing (A22) recurrent infection (A23) and otitis media (A24) It is particularly interesting to note the strong positive correlations obtained between preoperative size of adenoids (A20) and the indication recurrent otitis media (A24) on the one hand and on the other number of siblings with ear nose and throat diseases (A09)

From Table 16 it will also be seen that year of birth (A02) shows significant positive correlations with relative size of adenoids (A20 and A32) as well as with recurrent infection as an indication for adenoidectomy (A23) This indicates that size of adenoids in relation to the nasopharynx decreases with increasing age.

Good agreement between clinical and radiographic assessments of the size of adenoids in relation to the nasopharynx is indicated by the high significant correlations ($r = \geq 0.60$) between the otologist's clinical assessments (A16) and the author's estimates (A20) and measurements (A32) on lateral cephalometric radiographs.

Summary

Table 16 shows that there are marked relationships between mode of breathing and size of adenoids. There are strong indications that mouth breathing is a consequence of enlarged adenoids on the posterior wall of the nasopharynx. The correlations in the table also indicate that size of adenoids decreases with increasing age and that there is good agreement between clinical and radiographic assessments of size of adenoids

Variables for anamnesis and clinical status correlated with airflow variables

Table 17 shows significant correlations between anamnesis and clinical status on the one hand and variables for nasal airflow measured at a differential pressure of 10 mm H_2O before and after nose drops on two occasions on the other The airflow measurements at differential pressures of 15 and 20 mm H_2O are not included in view of the strong intercorrelations displayed by these and the measurements at 10 mm H_2O ($r > 0.97$) Variable A12, Open or closed mouth, is not included either as it correlates strongly ($r = 0.87$) with variable A15

There is a large number of correlations which are significant at the 1% level ($r > 0.20$) Most of them concern relationships between anamnesis and clinical status variables for obstructed nose breathing (A05 A13–16 A18) on the one hand and nasal airflow before (A67) as well as after (A70) nose drops at the first examination on the other These relationships could not be demonstrated at the second examination, which was only to be expected

the skeleton and lips on the other

A108 NL/NSL
A109 ba-s-pm
A110 n-s-ba
A111 $\frac{\text{Face width} \quad 100}{\text{Face height}}$
A113 $\frac{\text{lo–lo} \quad 100}{\text{n–gn}}$
A114 $\frac{\text{n–s} \quad 100}{\text{n–gn}}$

A115 $\frac{\text{ar'–pm} \quad 100}{\text{n–gn}}$
A116 $\frac{\text{n–sp'} \quad 100}{\text{n–gn}}$
A117 $\frac{\text{sp pm} \quad 100}{\text{n–sp}}$
A118 $\frac{\text{ho–ba} \quad 100}{\text{pm–ba}}$
A119 $\frac{\text{s–ba} \quad 100}{\text{n–s}}$

A120 $\frac{\text{pm–ba} \quad 100}{\text{ho} \perp \text{pm–ba}}$
A121 pm–ho
A122 ba–ho
A123 ho ⊥ pm–ba pm–ba ⟂
A124 s–n–ba
A125 pm–ho–ba
A127 s–ho
A128 Body height

100	101	102	103	104	105	106	107	108	109	110	111	113	114	115	116	117	118	119	120	121	122	123	124	125	127	128
44	.51								.31		.36	.37	.35			.23		.29		−.30		−.38		.20	41	.86
							.22				.21															
						.21	.23		.24		.30	.27	.25	.25					−.23				.21	.22		
						.30	.29		.25		.38	.35	.36	.33		.24	.22						.26	.25		
							.21		.23	.23														.25		
.25						.24	.24	.21					.20	.25		.22										
									.21				.29	.29		.22									.22	
			.23			.26	.25		.22		.20		.25	.27		.25							−.28			
						.28	.25		.23		.22	.22	.30	.29		.24							−.24			
		.21	.25	.22		.35	.35		.32		.34	.32	.35	.36		.26	.22						−.32	.28		
						.25	.28		.21		.27	.26	.23	.27									−.24	.22		
							.22				.24															
																				−.24						

Summary

It will be seen from Table 18 that the age variable is significantly correlated with the majority of skeleton and lip variables. The variables for mode of breathing also display strong correlations with a large number of skeleton and lip variables. Thus, children who are mouth breathers and/or have nasal obstructions display a high face height with a large angle between the reference lines in the upper and lower jaws, a short nasopharynx in the sagittal plane, a small index for face width/face height, a small face depth as well as long upper and lower lips.

Variables for anamnesis and clinical status correlated with variables for tongue position

Table 19 shows the significant correlations between anamnesis and clinical status variables on the one hand and variables for tongue position (A129–131) on the other As in previous tables, variable A12 is excluded as it correlates strongly with A15

The significant correlations in Table 19 concern the relationship between variables for mode of breathing (A05 A13–16) and the shortest distance between the tongue and pterygomaxillare (A129) and the soft palate (A131)

Summary

Table 19 indicates that a low tongue position is associated with mouth breathing and nasal obstruction.

Correlations between dentition variables

Table 20 presents simple correlations between all pairs of dentition variables with the exception of A51 Width of upper arch between the first deciduous molars, which is not included as it correlates strongly with A49

There is a very large number of correlations which are significant at the 1% level (i.e. $r >$

Table 18 *Correlations between variables for anamnesis and clinical status on the one hand and variables fo*
The table only shows correlation coefficients that are significant at the 1 % level ($r \geq 0.20$)

A80 Face width
A82 Nose width over alae nasii
A83 Nose width above alae nasii
A84 Height of upper lip
A85 n–s
A86 s–ba
A87 n–ba
A88 n–gn
A89 n–sp

A90 sp–gn
A91 ss–pm
A92 pm–ba
A93 bo ⊥ pm–ba
A94 s–pm
A95 s ⊥ pm–ba
A96 Height of upper lip
A97 Height of lower lip
A99 lo–lo

A100 bch bch
A101 bch–bch / pm–ba bo ⊥ pm–ba
A102 s–n–ss
A103 s–n–sm
A104 s–n–ss > 82°
A105 ss–n–sm
A106 ML/NSL
A107 ML/NL

Variable	A	80	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	99
Age	02	–45	–.37	.6	.37	–.27	–46	41	–.59	–60	.38	45		.35	.50	.21	.33	.36	.26
Sex	03					–.35		–.26					–.20					.21	
Mode of breathing	04								.28		.21					.23	.32	.5	
Mouth in sleep	05								.36	.24	.25			.20			.27	.27	
Infec. in ear n. & throat	06																	.24	
Allergy	07																		
Prev adenoidectomy	08																		
Siblings ear n. & throat dis.	09																		
Prolonged finger sucker	10								–.22									.28	
Obstruc. nose breathing, left	13								.20				–.25						
Obstruc. nose breathing, right	14								.21				.26						
Mouth breathing	15								.32		.25		.29				.23	.29	
Enlarged adenoids	16								.20									.21	
Large tonsils	17																	.4	
Swollen nasal mucosa	18																		
Septum deviation	19							.2											

of the bony nasopharynx (A92) Nor is age significantly correlated with the variables representing the angles s–n–ss and ss–n–sm (A102 and A103 respectively)

There are also several significant correlations between sex (A03) and the skeleton and lip variables Thus, boys have higher values than girls for variables concerning length of cranial base (A85 A87) sagittal depth of bony nasopharynx (A92) length of upper and lower lip (A96 and A97 respectively) and angle between lower and upper jaw (A107) The girls, on the other hand, have a significantly higher index for face width/face height (A111)

A large number of significant correlations concern variables connected with obstructed nose breathing (A04–05 A13–16) on the one hand and on the other variables concerning face height (A88 A106 A111 A114 A115) sagittal depth of face (A124) sagittal depth of nasopharynx (A92, A109 A125) angle between upper and lower jaws (A107) index for face width/face height (A111 A113) and face depth/face height (A114–115) Thus children who are mouth breathers (A04 A15) and/or have nasal obstructions (A13–14 A16) have a high face height with a large angle between the upper and lower jaws a short nasopharynx in the sagittal plane, a small index for face width/face height and a small face depth Mouth breathers also appear to have long upper and lower lips.

Table 18 also shows that prolonged finger suckers (A10) are correlated with the variables for face height (A88) length of lower lip (A97) sagittal depth of bony nasopharynx (A109) and the indexes for face depth/face height (A114–115 A117) The sign of these correlations is the opposite of that for the corresponding correlations with the variables for mode of breathing mentioned above. This is in keeping with the fact that groups 1 2 and 3 have the highest proportion of finger suckers (cf Table 7 p 38)

Table 10. Correlations between all pairs of dentition variables

The table only shows correlation coefficients that are significant at the 1 % level ($r \geq 0.20$)

Variable		A	42	43	44	45	46	47	48	49	50	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66
m & am prop. on OL		42																								
Freeway space prop.		43																								
OL/ML		44																								
OL/NSL		45																								
IL_s/NSL		46				40																				
IL_s/IL_t		47					70																			
IL_t/ML		48			45	–.24		.38																		
Arch width M_1–M upper		49				.26	.26	.27	.30																	
Arch width M M_1 lower		50								.58																
Arch width 04–04 lower		52					.37	43	46	.60	45															
Arch length, upper		53	.31				.37	45		.38		44														
Arch length, lower		54					.33	–.48	.39	–.3			.63													
Overjet		55	.29					–.26					.33													
Overbite		56			–.30					.26																
Sagittal rel. M M right		57	.26						.32					.25	44											
Sagittal rel. M_1–M left		58							.25					.26	.35		.58									
Crossbite		59								.29						–.22										
IL of pal. vault at M M		60														.26										
Space diff. of upper arch		61					.28	.33		44	.29	.30														
Space diff. of lower arch		62						.27		.33	41	.34		.26							.52					
Lower arch width M_1–M_1 / Upper arch width M M	100	63							.34	.39	.53					48			60							
Lower arch width 04–04 / Upper arch width 04–04	100	64								.30									41				49			
Upper arch length 100 / Upper arch width M_1–M		65						.29		.38	–.25		66	.27	.32											
IL of pal. vault M_1–M_1 / Upper arch width M M	100	66			.30					35										89	.33					

Table 19 *Correlations between variables for anamnesis and clinical status on the one hand and variables for tongue position on the other*

The table only shows correlation coefficients that are significant at the 1 % level ($r \geq 0.36$)

Variable	A	pm–t preop rest position 129	ba–t preop. rest position 130	$\frac{pm\text{–}v}{2}$–t_4 preop. rest position 131
Age	02			
Sex	03			
Mode of breathing	04			
Mouth in sleep	05	40		42
Infec. in ear n & throat	06			
Allergy	07			
Prev adenoidectomy	08			.38
Siblings ear n & throat dis.	09			
Prolonged finger-sucker	10			
Obstruc. nose breathing, left	13	40		48
Obstruc. nose breathing, right	14	47		.57
Mouth breathing	15	47		45
Enlarged adenoids	16	47		45
Large tonsils	17			
Swollen nasal mucosa	18			
Septum deviation	19			

0 20) The variables that express the inclination of the upper and lower incisors in relation to the nasion-sella line (A46) and the mandibular line (A48) as well as their mutual inclination (A47) display high correlations with the variables for arch width (A49 A52, A63 and A64) and arch length (A53–54 and A65) This indicates that retroclination of the incisors is more frequent in upper and/or lower arches that are narrow and short.

Width of upper arch between the first molars (A49) is significantly correlated to other variables for arch width (A50 A52 A59 and A63–64) as well as to variables that express the length of the upper and lower arches (A53 and A54 respectively) and those for the space difference of the upper and lower arches (A61 and A62 respectively)

The variables for upper arch width also display significant positive and negative correlations respectively with those for overbite (A56) and the angle between the occlusal and nasion sella lines (A45) The correlations with height of palatal vault (A60 A66) on the other hand are not significant. This indicates that a narrow upper arch is frequently associated with upper and lower arches that are short and crowded The incidence of crossbite also appears to be high among children with a narrow upper jaw as do the incidences of overbite and a large angle between the occlusal and nasion-sella lines.

The only significant correlation for height of palatal vault (A60) in Table 20 concerns a positive relationship with overbite (A56)

A small overbite (A56) also appears to be common in cases with crossbite (A59) judging from the significant negative correlation between these variables. There is also a significant negative correlation between overbite (A56) and the angle between the occlusal and mandibular lines (A44) The latter variable in its turn displays a significant negative correlation with the angle between the lower incisors and the mandibular line (A48)

Overjet (A55) shows significant negative correlations with the variables that express the sagittal distance between the mesial surfaces of the first upper and lower molars on the right and left (A57 and A58 respectively) In keeping with the definitions of the latter variables, positive values were noted when the

Table 22. *Correlations between dentition variables and airflow variables*

The table only shows correlation coefficients that are significant at the 1% level ($r \geq 0.20$)

Variable	A	Preop. airflow before nose drops 67	Preop. airflow after nose drops 70	Postop. airflow before nose drops 73	Postop. airflow after nose drops 76
is & im proj on OL	42				
Freeway space preop.	43				−.30
OL/ML	44				
OL/NSL	45	−.24	−.38		−.35
IL_s/NSL	46	.31	.27		.25
IL_s/IL_i	47				
IL_i/ML	48	.28	.28		
Arch width M -M upper	49		.25	.28	.32
Arch width M_1–M lower	50				
Arch width 04–04 lower	52				
Arch length, upper	53				
Arch length, lower	54	.26			
Overjet	55				
Overbite	56				
Sagittal rel. M_1–M right	57				
Sagittal rel. M –M left	58				
Crossbite	59				
H. of pal. vault at M_1–M	60				
Space diff. of upper arch	61				
Space diff. of lower arch	62				
Lower arch width M_1–M_1 100 / Upper arch width M -M	63				−.25
Lower arch xth 04–04 100 / Upper arch width 04–04	64				
Upper arch length 100 / Upper arch width M_1–M	65				
H. of pal. vault M_1 M_1 100 / Upper arch width M -M	66				

do not display any significant correlations with freeway space between the upper and lower jaws with the lower jaw in the rest position (A43)

Summary

The significant correlations shown in Table 20 indicate that

narrow short arch in the upper as well as the lower jaw frequently involves retroclination of the incisors in relation to the nasion-sella line and the mandibular line·

narrow upper arch occurs frequently in short, crowded lower and upper jaws and is frequent ly associated with small overbite and a large angle between the occlusal and nasion-sella lines

small overbite is common in children with crossbite

large overjet occurs frequently among children with a postnormal relation between the upper and lower first molars and a long upper arch short lower arch is frequently associated with retroclined upper and lower incisors, large sagittal distance between the mesial surfaces of the lower and upper first molars, crowded lower jaw and a short upper arch.

Dentition variables correlated with adenoid variables

Correlations between dentition variables and ade noid variables are shown in Table 21 Variables A34–36, A51 A38–39 and A40–41 are not included as they correlate strongly with A33 A26–27 A49 A29–30 and A26–27 respec tively

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Table 21 *Correlations between dentition variables and adenoid variables*

The table only shows correlation coefficients that are significant at the 1 % level (r ≥ 0.20)

A20 Ad. size before adenoidectomy
A21 Ad. size after adenoidectomy
A22, A23, A24, A25 Indication for adenoidectomy: obstr nose breathing; recurrent infection; recurrent otitis media; allergy
A26 ad –ba preop
A27 ad₁–ba postop.
A28 ad –ba difference
A29 ad₁–ho preop.
A30 ad ho postop.
A31 ad₁–ho difference
A32 $\frac{\text{Ad. area} \cdot 100}{\text{pm–ho–ba–pm}}$ preop.
A33 $\frac{\text{Ad area} \cdot 100}{\text{pm–ho–ba–pm}}$ postop.
A37 $\frac{\text{Ad area} \cdot 100}{\text{pm–ho–ba–ho'–pm}}$ difference

Variable	A	20	21	22	23	24	25	26	27	28	29	30	31	32	33	37
ss & sm proj. on OL	4															
Freeway space preop	43															
OL/ML	44			.25												
OL/NSL	45	.27		.24							.23			.27		
IL_s/NSL	46	–.27		–.26										–.26		
IL_s/IL_i	47	.34		.36	.30			.30			.27			.33		
IL_i/ML	48	–.43		–.47	–.23			.33			–.36			–.42		
Arch width M –M upper	49	–.27												–.30		
Arch width M –M lower	50															
Arch width 04–04 lower	52															
Arch length upper	53															
Arch length lower	54			–.27												
Overjet	55															
Overbite	56															
Sagittal rel. M M right	57															
Sagittal rel. M –M left	58															
Crossbite	59			.25												
H of pal vault at M₁–M	60															
Space diff of upper arch	61															
Space diff of lower arch	62															
Lower arch width M M · 100 / Upper arch width M –M₁	63	.32		.27	.23									.23		
Lower arch width 04–04 · 100 / Upper arch width 04–04	64															
Upper arch length · 100 / Upper arch width M₁–M	65															
H of pal vault M₁ M₁ · 100 / Upper arch width M M	66															

mesial surface of the lower molar was more mesial than the corresponding surface of the upper molar These findings indicate that large overjet is significantly correlated to a postnormal relation between the first upper and lower molars This relationship also agrees with the significant positive correlation between overjet (A55) and the sagittal distance between subspinale and supramentale projected onto the occlusal line (A42)

Overjet (A55) also shows a significant correlation with length of upper arch (A53) but not with length of lower arch (A54)

In addition to the significant correlations already mentioned with variables for the inclination of the upper and lower incisors (A46, A47 and A48) and for width of upper arch (A49) length of lower arch (A54) is also significantly correlated with length of upper arch (A53) sagittal relation between the mesial surfaces of the upper and lower first molars (A57–58) and space difference of lower arch (A62)

Thus, a short lower arch appears to be frequently associated with retroclination of the upper and lower incisors, a large sagittal distance between the mesial surfaces of the upper and lower first molars, a crowded lower jaw and short length of upper arch

The dentition variables listed in Table 20

NL/NSL
ba–s–pm
a–s–ba
(Face width · 100) / Face height
(lo–lo · 100) / n–gn
(n–s · 100) / n–gn

A115 (sa'–pm · 100) / n–gn
A116 (n–sp' · 100) / n–gn
A117 (sa'–pm · 100) / n–sp
A118 (ho–ba · 100) / pm–ba
A119 (s–ba · 100) / n–s

A120 (pm–ba · 100) / ho ⊥ pm–ba
A121 pm–ho
A122 ba–ho
A123 ho ⊥ pm–ba pm–ba ½
A124 sa–n–ba
A125 pm–ho–ba
A127 s–ho
A128 Body height

0	101	102	103	104	105	106	107	108	109	110	111	113	114	115	116	117	118	119	120	121	122	123	124	125	127	128
					.36																					
	.30							.34																		
						.73	.74				.48	.44	–.47	.47	.37											
	.21	.44	.65	.39	.21	.59	.35	.28			.25	.22		–.4		–.33		.22		.20		.22	–.31		–.27	
		.32	.48	.26																			.25		.24	
		.25																					.25			
		.31			.29	.52	.53		.27		.34	.35	.36	.46	.33	.26				.30			.37			
13	.42	.25	.35	.32		.29	.25													.32		.35				.28
36					.24																					
57	.27	.27	.29	.28		.35	.28				.28						.34								.36	.41
																				.31						
		.23		.23										.28		.29				.24			.30			
			.27		.30																	.24			.22	
	.25					.25	.31								.33					.23					.28	.39
					.29																					
					.29																					
.57	.38								.25		.27	.27	.36	.28		.23		.29		.24		.26			.42	.62
				.20										.22												
				.23		.21																				
			.23												.24					.23			.25			
						.29	.33																			
.31											.33	.37	.49	.38		.25		.30							.37	.60

A32) and those for arch width between first molars (A49) and the index for widths of lower and upper jaws between first molars (A63). Children with enlarged adenoids on the posterior wall of the nasopharynx thus appear prone to have a narrow upper arch and crossbite.

Summary

The significant correlations in Table 21 between dentition and adenoid variables support the assumption of a relationship between the occurrence of adenoids and special characteristics of the dentition. The relationship indicates that children with adenoids frequently have a narrow upper jaw, crossbite or a tendency to crossbite, retroclined upper and lower incisors, a short lower jaw and large angles between the occlusal line and the mandibular and nasion-sella lines.

Dentition variables correlated with airflow variables

Significant correlations between dentition variables and variables for nasal airflow measured in lit/min at a differential pressure of 10 mm H_2O before and after nose drops on two occasions are shown in Table 22. Variable A51 is not included as it correlates strongly with variable A49.

Table 23. *Correlations between dentition variables and variables for the skeleton and lips*

The table only shows correlation coefficients that are significant at the 1 % level ($r \geq 0.20$)

A80 Face width	A90 sp gn	A100 bch–bch
A82 Nose width over alae nasil	A91 ss pm	A101 bch–bch ho ⊥ pm–ba / pm–ba
A83 Nose width above alae nasil	A92 pm–ba	A102 s–n–ss
A84 Height of upper lip	A93 ho ⊥ pm–ba	A103 s–n–sm
A85 n–s	A94 s–pm	A104 s–n–ss > 8?°
A86 s–ba	A95 s ⊥ pm–ba	A105 ss–n–sm
A87 n–ba	A96 Height of upper lip	A106 ML/NSL
A88 n–gn	A97 Height of lower lip	A107 ML/NL
A89 n–sp	A99 lo–lo	

Variable	A	80	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	99
ss & sm proj on OL	42												-.2						
Freeway space preop	43																		
OL/ML	44								.37		.38						.25	.34	
OL/NSL	45						-.24			.26			-.35		-.30				
ILs/NSL	46																		
ILs/ILi	47																		
ILi/ML	48							.23	-.23			.35	35						
Arch width M_1–M upper	49	.33	.27			.25	.23	.27				.30	.28		.37				
Arch width M_1–M lower	50	.24													.22				.27
Arch width 04–04 lower	52	.54	43	.32								.38			.39				41
Arch length, upper	53		.24									.34			.26				
Arch length, lower	54		.25									.39	.24						
Overjet	55					.22	.24	.28				.31			.26				
Overbite	56	.32				.23	.28	.28		.34		.34			.33				
Sagittal rel. M M right	57					-.23													.22
Sagittal rel. M_1–M left	58																		
Crossbite	59																.20		
H of pal. vault at M_1–M	60	46	.28		.35		41	.35	.59	46	41	.26			.38		.38	.-7	.39
Space diff of upper arch	61																		
Space diff of lower arch	62			.24															
Lower arch width M_1–M_1 / Upper arch width M M · 100	63												.29				.29		
Lower arch width 04–04 / Upper arch width 04–04 · 100	64																		
Upper arch length / Upper arch width M_1–M · 100	65										.26								
H of pal. vault M_1–M_1 / Upper arch width M –M · 100	66	40			.38		.35	.28	63	4	49						.50	.32	.33

There is a considerable number of significant correlations ($P < 0.01$) The majority concern the dentition variables that express the inclination of upper and lower incisors (A46–48) and the angle between the occlusal and nasion-sella lines (A45) on the one hand and, on the other variables for size of adenoids in relation to the nasopharynx (A20 A32) and obstructed nose breathing as an indication for adenoidectomy (A22)

Thus, children whose adenoids are large in relation to the nasopharynx and who also suffer from nasal obstruction frequently display retroclination of the upper and lower incisors as well as a large angle between the occlusal and nasion-sella lines. Obstructed nose breathing as an indication for adenoidectomy (A22) is also significantly correlated with length of lower jaw (A54) crossbite (A59 A63) and the angle between the occlusal and mandibular lines (A44)

Besides having retroclined upper and lower incisors, children who undergo adenoidectomy on account of obstructed nose breathing frequently display a short lower jaw a large angle between the occlusal and mandibular lines and crossbite

It is also interesting to note the significant correlations between variables for size of adenoids in relation to the nasopharynx (A20

The inclination of the upper incisors in relation to the nasion-sella line (A46) shows significant positive correlations with the angles s–n–ss and s–n–sm (A102, A104 and A103 respectively) as well as the angle ss–n–ba (A124).

A greater number of significant correlations are found for the inclination of the lower incisors in relation to the mandibular line (A48) and the skeleton and lip variables, i.e. variables for depth of face (A87 A91), face height (A88), angle of mandibular line in relation to nasion-sella line (A106) and nasal line (A107) sagittal depth of bony nasopharynx (A92, A109), distance between pterygomaxillare and hormion (A121), and the angles s–n–ss (A102) ss–n–ba (A124) and ss–n–sm (A105) Thus, children with retroclined lower incisors frequently have small face depth, large face height, large angles between the mandibular and the nasion-sella (A106) and nasal lines (A107) small sagittal depth of nasopharynx, low height of posterior choanal aperture and small values for the angles s–n–ss and ss–n–sm.

The variables for arch width (A49 A50 A52) also display a large number of significant correlations with the skeleton and lip variables. However as these dentition variables display relatively strong intercorrelations (≥0.58) the present account will be confined to the one with the greatest number of significant correlations with the skeleton variables, namely A49 Upper arch width between first molars.

Variable A49 is significantly correlated to the variables for face width (A80) nose width over alae nasi (A82), width (A100) and height (A121) of posterior choanal aperture, face depth (A87 A91), depth of anterior cranial base (A85), angle of mandibular line in relation to the nasion-sella line (A106) and to the nasal line (A107) posterior upper face height (A94) volume and sagittal depth of bony nasopharynx (A101 and A92 respectively), the angles s–n–ss (A102, A104), and s–n–sm (A103), and body height (A128). Thus, children with a narrow upper arch between the first molars more frequently have a narrow face and nose a short face and cranial base depth, low posterior upper face height, a low and narrow posterior choanal aperture, a small volume and sagittal depth of the nasopharynx, large angles between the mandibular and the nasion-sella and nasal lines, small values for the angles s–n–ss and s–n–sm, and small body height.

Length of upper arch (A53) shows significant correlations with only a few skeleton variables, viz. nose width (A82), face depth (A91), posterior upper face height (A94) and height of posterior choanal aperture (A121) All these correlations are positive.

Length of lower arch (A54) is significantly correlated not only with the same skeleton variables as length of upper arch but also with variables for sagital depth of bony nasopharynx (A92) the angle s–n–ss (A102, A104) the angle ss–n–ba (A124), and the index for face depth/face height (A115 A117). These correlations are also positive

Overjet (A55) is also significantly correlated with several skeletal variables, viz. face depth (A91) cranial base depth (A85 A87) posterior upper face height (A86 A94 A127), the angle s–n–sm (A103), the angle ss–n–sm (A105) and the sagittal cross-section of the bony nasopharynx (A123) Thus, children with large overjet frequently have a large face depth, large cranial base depth, large posterior upper face height, a tendency to small values for the angle s–n–sm, large values for the angle ss–n–sm, and a large sagittal cross-section of the bony nasopharynx.

Overbite (A56) is significantly correlated with the variables for face width (A80) face depth (A91), cranial base depth (A85 A87) anterior and posterior upper face height (A89 A116 and A86, A94 A127 respectively) height of posterior choanal aperture (A121), volume of bony nasopharynx (A101) angle of mandibular line in relation to nasion-sella line (A106) and to nasal line (A107), and body height (A128) Thus, children with a small overbite more frequently have a small face width small face and cranial base depth, small anterior and posterior upper face height, low posterior choanal aperture, small volume of

The significant correlations chiefly refer to the relationship between variables for inclination of upper and lower incisors (A46 and A48 *respectively*) and the angle between the occlusal and nasion-sella lines (A45) on the one hand and airflow variables before adenoidectomy before (A67) as well as after (A70) nose drops on the other Variables A46 and A45 also show significant correlations with A76 Airflow after nose drops after adenoidectomy The correlations indicate that retroclination of upper and lower incisors and a large angle between the occlusal and nasion-sella lines are more common among children with a low nasal *airflow*

Width of upper arch between first molars (A49) is also significantly correlated to airflow after nose drops before adenoidectomy (A70) as well as to airflow before and after nose drops one month after adenoidectomy (A73 and A76 respectively) A narrow upper arch is thus common among children with a low nasal airflow

Length of lower arch (A54) also displays a significant positive correlation to nasal airflow before nose drops before adenoidectomy (A67) Crossbite or a tendency to crossbite (A63) displays a significant negative correlation with nasal airflow after nose drops after adenoidectomy (A76)

Summary

The correlations in Table 22 show that low nasal *airflow is common among children with* a narrow upper arch, retroclination of upper and lower incisors, a large angle between the occlusal and nasion-sella lines, a short lower arch and crossbite

Dentition variables correlated with skeleton and lip variables

Significant correlations between dentition variables and variables *for the* skeleton and lips are shown in Table 23 Variables A51 A81 A98 A112 and *A126* are *not* included as they correlate strongly with variables A49 A88 A99 A113 and A87 respectively

There is a very large number of significant correlations ($P < 0\ 01$)

An interesting finding is the significant positive correlation for the distance between subspinale and supramentale projected onto the occlusal line (A42) in relation to the sagittal depth of the bony nasopharynx (A92)

Variable A42 also shows a significant correlation with the angle *ss–n–sm (A105) but* the coefficient ($r = 0\ 36$) is not sufficiently high for these variables to be regarded as interchangeable

The angle between the occlusal and mandibular lines (A44) shows significant positive correlations with face height (A88 A90) the angle of the mandibular line in relation to the nasion-sella line (A106) and the nasal line (A107)

More noteworthy correlations are the significant positive coefficients between A44 and the variables for height of upper lip (A96) and lower lip (A97)

The angle between the occlusal and nasion-sella lines (A45) is significantly correlated to the following variables, anterior (A89) and posterior upper face height (A86 A94 A127), angle of the mandibular line in relation to the nasion-sella line (A106) and to the nasal line (A107) sagittal depth (A92) and volume (A101) of the bony nasopharynx, distance between pterygomaxillare and hormion (A121) the angles s–n–ss and s–n–sm (A102, A104 and A103 respectively) and the angle ss–n–sm (A105)

These correlations indicate that children with a large angle between the occlusal and nasion-sella lines frequently have a high anterior but low posterior face height, a large angle for the mandibular line in relation to the nasion sella and nasal lines, small sagittal depth and volume of nasopharynx, low posterior choanal aperture a tendency to small values for the angles s–n–ss and s–n–sm and a high value for the angle ss–n–sm

The inclination of the upper incisors in relation to the nasion-sella line (A46) shows significant positive correlations with the angles s–n–ss and s–n–sm (A102, A104 and A103 respectively) as well as the angle ss–n–ba (A124)

A greater number of significant correlations are found for the inclination of the lower incisors in relation to the mandibular line (A48) and the skeleton and lip variables, i.e. variables for depth of face (A87 A91), face height (A88) angle of mandibular line in relation to nasion-sella line (A106) and nasal line (A107), sagittal depth of bony nasopharynx (A92, A109) distance between pterygomaxillare and hormion (A121), and the angles s–n–ss (A102), ss–n–ba (A124) and ss–n–sm (A105) Thus, children with retroclined lower incisors frequently have small face depth, large face height, large angles between the mandibular and the nasion-sella (A106) and nasal lines (A107) small sagittal depth of nasopharynx, low height of posterior choanal aperture and small values for the angles s–n–ss and ss–n–sm.

The variables for arch width (A49 A50 A52) also display a large number of significant correlations with the skeleton and lip variables. However as these dentition variables display relatively strong intercorrelations ($r > 0.58$) the present account will be confined to the one with the greatest number of significant correlations with the skeleton variables, namely A49 Upper arch width between first molars.

Variable A49 is significantly correlated to the variables for face width (A80), nose width over alae nasi (A82), width (A100) and height (A121) of posterior choanal aperture, face depth (A87 A91), depth of anterior cranial base (A85), angle of mandibular line in relation to the nasion-sella line (A106) and to the nasal line (A107), posterior upper face height (A94), volume and sagittal depth of bony nasopharynx (A101 and A92 respectively), the angles s–n–ss (A102, A104), and s–n–sm (A103), and body height (A128) Thus, children with a narrow upper arch between the first molars more frequently have a narrow face and nose a short face and cranial base depth, low posterior upper face height, a low and narrow posterior choanal aperture, a small volume and sagittal depth of the nasopharynx, large angles between the mandibular and the nasion-sella and nasal lines, small values for the angles s–n–ss and s–n–sm, and small body height.

Length of upper arch (A53) shows significant correlations with only a few skeleton variables viz. nose width (A82), face depth (A91), posterior upper face height (A94) and height of posterior choanal aperture (A121) All these correlations are positive.

Length of lower arch (A54) is significantly correlated not only with the same skeleton variables as length of upper arch but also with variables for sagittal depth of bony nasopharynx (A92), the angle s–n–ss (A102, A104), the angle ss–n–ba (A124), and the index for face depth/face height (A115 A117) These correlations are also positive.

Overjet (A55) is also significantly correlated with several skeletal variables, viz. face depth (A91), cranial base depth (A85 A87), posterior upper face height (A86, A94 A127), the angle *s–n–sm (A103)* the angle ss–n–sm (A105) and the sagittal cross-section of the bony nasopharynx (A123) Thus, children with large overjet frequently have a large face depth large cranial base depth, large posterior upper face height, a tendency to small values for the angle s–n–sm, large values for the angle ss–n–sm, and a large sagittal cross-section of the bony nasopharynx.

Overbite (A56) is significantly correlated with the variables for face width (A80) face depth (A91), cranial base depth (A85 A87) anterior and posterior upper face height (A89 A116 and A86, A94 A127 respectively) height of posterior choanal aperture (A121) volume of bony nasopharynx (A101), angle of mandibular line in relation to nasion-sella line (A106) and to nasal line (A107), and body height (A128). Thus, children with a small overbite more frequently have a small face width, small face and cranial base depth, small anterior and posterior upper face height, low posterior choanal aperture, small volume of

bony nasopharynx, large angles between the mandibular and the nasion-sella and nasal lines, and small body height.

The variables for the sagittal relation between the upper and lower first molars on the right and left sides (A57 and A58 respectively) display significant negative correlations with the variable for the angle ss–n–sm (A105) In keeping with the definitions of variables A57 and A58 a positive sign indicates that the mesial surface of the lower molar is more mesial than the corresponding surface of the upper molar Thus, a small value for the angle ss–n–sm tends to be accompanied by a large sagittal distance between the mesial surfaces of the lower and upper molars

The dentition variable that has the greatest number of significant correlations with the skeletal variables in Table 23 is A60 Height of palatal vault. This is significantly correlated to breadth of face and nose (A80 A99 and A82 respectively) face depth (A87 A91) total face height (A88) anterior and posterior upper face height (A89 and A86 A94 A127 respectively) anterior lower face height (A90) width and height of posterior choanal aperture (A100 and A121 respectively) volume and sagittal cross-section of bony nasopharynx (A101 and A123 respectively) height of upper and lower lip (A84 A96 and A97 respectively) body height (A128) and the indexes for face width/face height (A111 A113) and face depth/face height (A115 A117) This indicates that a high palatal vault is common in children with a wide face and nose large face depth large anterior and posterior face height, wide and high posterior choanal aperture high and large bony nasopharynx, long upper and lower lips, large body height and small indexes for face breadth/face height and face depth face height.

The index for height of palatal vault and upper arch width between first molars (A66) also displays a large number of significant correlations with the skeletal variables in Table 23 Almost all the significant correlations are the same as those obtained for height of palatal vault alone (A60) suggesting that this variable dominates the index variable.

The variables A61 and A62, which express the space difference in the upper and lower jaw respectively display only a few significant correlations with the skeletal variables, the only one of interest here being the positive correlation with the angle s–n–ss > 82 (A104)

Variable A63 which is an index between lower and upper arch widths between the first molars and can also be said to express the presence or absence of crossbite, is significantly correlated with sagittal depth of bony nasopharynx (A92) height of upper lip (A96) the angle s–n–ss (A102) the index for anterior upper face height and total face height (A116) height of posterior choanal aperture (A121), and the angle ss–n–ba (A124) Thus, children with crossbite as a result of the lower arch being wider than the upper at the first molars, frequently have a small sagittal depth of the bony nasopharynx, low posterior choanal aperture long upper lip a tendency to small values for the angle s–n–ss and a small anterior upper face height in relation to total face height

Summary

The majority of dentition values display significant correlations with the variables for the facial skeleton and lips in Table 23 These correlations show that:

retroclined upper incisors are common in children with small values for the angles s–n–ss and s–n–sm

retroclined lower incisors are common in children with small face depth, large face height, large angles between the mandibular line and the nasion sella and nasal lines, small sagittal depth of nasopharynx low posterior choanal aperture, and a tendency to small values for the angles s–n–ss and ss–n–sm

a narrow upper arch between the first molars is common among children with a narrow face and nose short face depth and cranial base depth small posterior upper face height, a low and narrow posterior choanal aperture small

Table 24 *Correlations between dentition variables and variables for tongue position*
The table only shows correlation coefficients that are significant at the 1% level (≥0.36)

Variable	A	pm–t$_4$ preop rest position 129	ba–t$_4$ preop. rest position 130	$\frac{pm-v}{2}$–t$_4$ preop rest position 131
ss & sm proj. on OL	42			
Freeway space preop.	43			
OL/ML	44	.37		
OL/NSL	45			
IL$_s$/NSL	46			
IL$_s$/IL$_i$	47			
IL$_i$/ML	48			
Arch width M$_1$–M upper	49			
Arch width M$_1$–M$_1$ lower	50			
Arch width 04–04 lower	52			
Arch length, upper	53			
Arch length, lower	54			
Overjet	55			
Overbite	56			
Sagittal rel. M$_1$–M right	57			
Sagittal rel. M$_1$–M left	58			
Crossbite	59			
H. of pal. vault at M$_1$–M	60		43	
Space diff. of upper arch	61			
Space diff of lower arch	62			.39
Lower arch width M$_1$–M$_1$ 100 / Upper arch width M –M$_1$	63			
Lower arch width 04–04 100 / Upper arch width 04–04	64			
Upper arch length 100 / Upper arch width M$_1$–M	65			
H. of pal. vault M$_1$–M$_1$ 100 / Upper arch width M$_1$–M	66	49	46	

nasopharynx, large angles between the mandibular line and the nasal and nasion-sella lines, small values for the angles s–n–ss and s–n–sm, and small body height,

large overjet is common among children with large face depth and cranial base depth, large posterior upper face height, a tendency to small values for the angle s–n–sm and large values for ss–n–sm, and large sagittal depth of nasopharynx

small overbite is common among children with small face width, small face depth and cranial base depth, small anterior as well as posterior upper face height, low posterior choanal aperture small nasopharynx, large angles between the mandibular line and the nasal and nasion-sella lines, and small body height

crossbite is common in children with small sagittal depth of nasopharynx, low posterior choanal aperture, long upper lip, a tendency to small values for the angle s–n–ss and a small anterior upper face height in relation to total face height.

Dentition variables correlated with variables for tongue position

Significant correlations between dentition variables and variables for tongue position are given in Table 24 Variable A51 is not included as it correlates strongly with variable A49

Only a few correlations are significant ($P < 0.01$) The majority are positive correlations between tongue position in relation to pterygomaxillare and basion (A129 and A130 respectively) on the one hand and variables for height

bony nasopharynx, large angles between the mandibular and the nasion-sella and nasal lines, and small body height

The variables for the sagittal relation between the upper and lower first molars on the right and left sides (A57 and A58 respectively) display significant negative correlations with the variable for the angle ss–n–sm (A105) In keeping with the definitions of variables A57 and A58 a positive sign indicates that the mesial surface of the lower molar is more mesial than the corresponding surface of the upper molar Thus a small value for the angle ss–n–sm tends to be accompanied by a large sagittal distance between the mesial surfaces of the lower and upper molars.

The dentition variable that has the greatest number of significant correlations with the skeletal variables in Table 23 is A60 *Height of* palatal vault This is significantly correlated to breadth of face and nose (A80 A99 and A82 respectively) face depth (A87 A91) total face height (A88) anterior and posterior upper face height (A89 and A86 A94 A127 respectively) anterior lower face height (A90) width and height of posterior choanal aperture (A100 and A121 respectively) volume and sagittal cross-section of bony nasopharynx (A101 and A123 respectively) height of upper and lower lip (A84 A96 and A97 respectively) body height (A128) and the indexes for face width/face height (A111 A113) and face depth/face height (A115 A117) This indicates that a high palatal vault is common in children with a wide face and nose large face depth large anterior and posterior face height, wide and high posterior choanal aperture high and large bony nasopharynx, long upper and lower lips, large body height and small indexes for face breadth/face height and face depth/face height

The index for height of palatal vault and upper arch width between first molars (A66) also displays a large number of significant correlations with the skeletal variables in Table 23 Almost all the significant correlations are the same as those obtained for height of palatal vault alone (A60) suggesting that this variable *dominates the index variable*

The variables A61 and A62, which express the space difference in the upper and lower jaw respectively display only a few significant correlations with the skeletal variables, the only one of interest here being the positive correlation with the angle s–n–ss > 82 (A104)

Variable A63 which is an index between lower and upper arch widths between the first molars and can also be said to express the presence or absence of crossbite, is significantly correlated with sagittal depth of bony nasopharynx (A92) height of upper lip (A96) the angle s–n–ss (A102) the index for anterior upper face height and total face height (A116), height of posterior choanal aperture (A121) and the angle ss–n–ba (A124) Thus, children *with crossbite as a result of the lower arch* being wider than the upper at the first molars, frequently have a small sagittal depth of the bony nasopharynx, low posterior choanal aperture, long upper lip a tendency to small values for the angle s–n–ss and a small anterior upper face height in relation to total face height

Summary

The majority of dentition values display significant correlations with the variables for the facial skeleton and lips in Table 23 These correlations show that:

retroclined upper incisors are common in children with small values for the angles s–n–ss and s–n–sm

retroclined lower incisors are common in children with small face depth large face height large angles between the mandibular line and the nasion sella and nasal lines, small sagittal depth of nasopharynx, low posterior choanal aperture and a tendency to small values for the angles s–n–ss and ss–n–sm

a narrow upper arch between the first molars is common among children with a narrow face and nose short face depth and cranial base depth small posterior upper face height a low and narrow posterior choanal aperture small

Table 24 *Correlations between dentition variables and variables for tongue position*

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Variable	A	pm–t_4 preop. rest position 129	ba–t_4 preop. rest position 130	$\frac{pm-v}{2}$–t_4 preop. rest position 131
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Arch width M_1–M_1 upper	49			
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Crossbite	59			
H. of pal. vault at M_1–M_1	60		43	
Space diff. of upper arch	61			
Space diff. of lower arch	62			.39
$\frac{\text{Lower arch width } M_1\text{–}M_1 \cdot 100}{\text{Upper arch width } M_1\text{–}M_1}$	63			
$\frac{\text{Lower arch width 04–04} \cdot 100}{\text{Upper arch width 04–04}}$	64			
$\frac{\text{Upper arch length} \cdot 100}{\text{Upper arch width } M_1\text{–}M_1}$	65			
$\frac{\text{H. of pal. vault } M_1\text{–}M_1 \cdot 100}{\text{Upper arch width } M_1\text{–}M_1}$	66	49	46	

nasopharynx, large angles between the mandibular line and the nasal and nasion-sella lines, small values for the angles s–n–ss and s–n–sm, and small body height

large overjet is common among children with large face depth and cranial base depth, large posterior upper face height, a tendency to small values for the angle s–n–sm and large values for ss–n–sm, and large sagittal depth of nasopharynx,

small overbite is common among children with small face width, small face depth and cranial base depth, small anterior as well as posterior upper face height, low posterior choanal aperture, small nasopharynx, large angles between the mandibular line and the nasal and nasion-sella lines, and small body height

crossbite is common in children with small sagittal depth of nasopharynx, low posterior choanal aperture, long upper lip a tendency to small values for the angle s–n–ss and a small anterior upper face height in relation to total face height.

Dentition variables correlated with variables for tongue position

Significant correlations between dentition variables and variables for tongue position are given in Table 24. Variable A51 is not included as it correlates strongly with variable A49

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bony nasopharynx large angles between the mandibular and the nasion-sella and nasal lines, and small body height

The variables for the sagittal relation between the upper and lower first molars on the right and left sides (A57 and A58 respectively) display significant negative correlations with the variable for the angle ss–n–sm (A105) In keeping with the definitions of variables A57 and A58 a positive sign indicates that the mesial surface of the lower molar is more mesial than the corresponding surface of the upper molar Thus a small value for the angle ss–n–sm tends to be accompanied by a large sagittal distance between the mesial surfaces of the lower and upper molars.

The dentition variable that has the greatest number of significant correlations with the skeletal variables in Table 23 is A60 Height of palatal vault. This is significantly correlated to breadth of face and nose (A80 A99 and A82 respectively) face depth (A87 A91) total face height (A88) anterior and posterior upper face height (A89 and A86 A94 A127 respectively) anterior lower face height (A90) width and height of posterior choanal aperture (A100 and A121 respectively) volume and sagittal cross section of bony nasopharynx (A101 and A123 respectively) height of upper and lower lip (A84 A96 and A97 respectively) body height (A128) and the indexes for face width/face height (A111 A113) and face depth/face height (A115 A117) This indicates that a high palatal vault is common in children with a wide face and nose, large face depth large anterior and posterior face height wide and high posterior choanal aperture, high and large bony nasopharynx, long upper and lower lips, large body height and small indexes for face breadth/face height and face depth/face height

The index for height of palatal vault and upper arch width between first molars (A66) also displays a large number of significant correlations with the skeletal variables in Table 23 Almost all the significant correlations are the same as those obtained for height of palatal vault alone (A60) suggesting that this variable dominates the index variable

The variables A61 and A62 which express the space difference in the upper and lower jaw respectively display only a few significant correlations with the skeletal variables, the only one of interest here being the positive correlation with the angle s–n–ss > 82 (A104)

Variable A63 which is an index between lower and upper arch widths between the first molars and can also be said to express the presence or absence of crossbite is significantly correlated with sagittal depth of bony nasopharynx (A92) height of upper lip (A96), the angle s–n–ss (A102) the index for anterior upper face height and total face height (A116), height of posterior choanal aperture (A121), and the angle ss–n–ba (A124) Thus, children with crossbite as a result of the lower arch being wider than the upper at the first molars, frequently have a small sagittal depth of the bony nasopharynx low posterior choanal aperture, long upper lip, a tendency to small values for the angle s–n–ss and a small anterior upper face height in relation to total face height

Summary

The majority of dentition values display significant correlations with the variables for the facial skeleton and lips in Table 23 These correlations show that

retroclined upper incisors are common in children with small values for the angles s–n–ss and s–n–sm

retroclined lower incisors are common in children with small face depth large face height, large angles between the mandibular line and the nasion-sella and nasal lines, small sagittal depth of nasopharynx low posterior choanal aperture and a tendency to small values for the angles s–n–ss and ss–n–sm

a narrow upper arch between the first molars is common among children with a narrow face and nose short face depth and cranial base depth small posterior upper face height a low and narrow posterior choanal aperture small

Table 26. *Correlations between adenoid variables and airflow variables*

The table only shows correlation coefficients that are significant at the 1% level (≥0.20)

Variable	A	Preop. airflow before nose drops 67	Preop. airflow after nose drops 70	Postop airflow before nose drops 73	Postop. airflow after nose drops 73
Ad. size before adenoidectomy	20	−.45	−.48		−.26
Ad. size after adenoidectomy	21				
Indication for adenoidectomy: obstr. nose breathing	22	−.33	−.33		
Indication for adenoidectomy: recurrent infection	23				
Indication for adenoidectomy: recurrent otitis media	24				
Indication for adenoidectomy: allergy	25				
ad$_1$–ba preop.	26				
ad$_1$–ba postop.	27				
ad$_1$–ba difference	28				
ad$_1$–ho preop.	29		−.28		
ad$_1$–ho postop.	30				
ad$_1$–ho difference	31				
$\frac{\text{Ad. area} \cdot 100}{\text{pm–ho–ba–pm}}$ preop.	32	−.25	−.32		
$\frac{\text{Ad. area} \cdot 100}{\text{pm–ho–ba–pm}}$ postop.	33				
$\frac{\text{Ad. area} \cdot 100}{\text{pm–ho–ba–ho'–pm}}$ difference	37				

The high significant correlations between riables for size of adenoids (A26–28 A29–) A37) are a consequence of the definitions ! these variables.

ummary

'able 25 shows that the radiographic assess- ıent of adenoid size is strongly correlated with denoid size measured planimetrically on late al cephalometric radiographs *It also shows* hat the children who underwent adenoidectomy for obstructed nose breathing have a larger size of adenoids than those who underwent the operation on account of recurrent otitis media.

Adenoid variables correlated with airflow variables

Table 26 shows significant correlations be- (een adenoid variables and variables for nasal airflow measured in lit/min at a *differential* pressure of 10 mm H_2O before and after nose drops before and after adenoidectomy Varia- bles A34–36 and A38–41 are not included as they correlate strongly with variables A33 A32, A27 A29–30, A26 and A27 respectively

Correlations that are significant at the 1% level chiefly refer to variables for size of adenoids (A20 A32) on the one hand and those for airflow before adenoidectomy (A67 A70) on the other Thus, children with enlarged adenoids frequently had a small nasal airflow

Obstructed nose breathing as an indication for adenoidectomy (A22) is significantly cor related at the 0.1% level with preoperative nasal airflow before and after nose drops (A67 and A70 respectively)

The clinical assessment of nose breathing in children who were adenoidectomized for nasal obstruction is thus in good agreement with the results of objective recordings of nasal airflow

Summary

The significant correlations in Table 26 be tween nasal airflow and size of adenoids support the assumption that enlarged adenoids in the nasopharynx impairs the ability to breath through the nose.

Table 25 *Correlations between most pairs of adenoid variables*

The table only shows correlation coefficients that are significant at the 1 % level ($r \geq 0.20$)

Variable	A	20	21	22	23	24	25	26	27	28	29	30	31	32	33	37
Ad size before adenoidectomy	20															
Ad. size after adenoidectomy	21	.24														
Indication for adenoidectomy: obstr nose breathing	22	64														
Indication for adenoidectomy: recurrent infection	23	40		.52												
Indication for adenoidectomy: recurrent otitis media	24	.27														
Indication for adenoidectomy: allergy	25															
ad_r–ba preop.	26	70		.50	34	26										
ad_r–ba postop	27		.51					49								
ad –ba difference	28	.38	– 36					.50	–.51							
ad_r–ho preop	29	72		.54	.31	.34		79								
ad_r–ho postop.	30	.32	62						.51		.53					
ad_r–ho difference	31		–.55						–.33	54	.36	– 60				
$\frac{\text{Ad area} \times 100}{\text{pm–ho–ba pm}}$ preop.	32	74		.54	.31	.26		.81		.51	.84	.32	.32			
$\frac{\text{Ad. area } 100}{\text{pm–ho–ba–pm}}$ postop	33		65					39	67		48	75	–.38	47		
$\frac{\text{Ad area } 100}{\text{pm–ho–ba–ho –pm}}$ difference	37	31	– 48					36	– 44	79		– 36	67	41	– 45	

of palatal vault (A60 A66) on the other Thus, not unexpectedly the distance between the tongue and the hard palate is usually large in children with a high palatal vault

There is also a significant correlation between space difference of lower arch (A62) and tongue position in relation to the soft palate (A131) indicating that children with a widely spaced lower dentition frequently have a large distance between the tongue and the soft palate.

The other significant correlation refers to a positive relationship for the angle between the mandibular and occlusal lines (A44) and the variable for tongue position in relation to pterygomaxillare (A129)

Summary

The significant correlations shown in Table 24 confirm the assumption of a relationship between certain characteristics of the dentition and tongue position The relationship indicates that the distance between tongue and hard palate is frequently large in children with a large angle between the occlusal and mandibular lines and a high palatal vault.

Correlations between adenoid variables

Significant correlations are presented in Table 25 for most pairs of adenoid variables. Variables A34–36 and A38–41 are not included as they correlate very strongly ($r \geq 0.85$) with variables A33 A32, A27 A29 A30 A26 and A27 respectively

There is a very large number of significant correlations ($P < 0.01$)

The radiographic estimate of adenoid size in relation to the bony nasopharynx (A20) is strongly correlated ($r = 0.74$) with the same relationship measured planimetrically on lateral radiographs (A32) Variable A20 is also strongly correlated ($r = 0.64$) to obstructed nose breathing as an indication for adenoidectomy (A22) whereas its correlation with recurrent otitis media as an indication for adenoidectomy (A24) is considerably weaker ($r = 0.27$) The difference between these two correlations is in line with the differences between the means for variable A20 in groups 4 and 5

The high significant correlation between obstructed nose breathing (A22) and recurrent infection (A23) as indications for adenoidectomy was to be expected

A108 NL/NSL
A109 ba-s-pm
A110 n-s-ba
A111 $\frac{\text{Face width} \cdot 100}{\text{Face height}}$
A113 $\frac{\text{lo-lo} \cdot 100}{\text{n-gn}}$
A114 $\frac{\text{n-s} \cdot 100}{\text{s-gn}}$

A115 $\frac{\text{sn'-pm} \cdot 100}{\text{n-gn}}$
A116 $\frac{\text{n-sp} \cdot 100}{\text{n-gn}}$
A117 $\frac{\text{sn'-pm} \cdot 100}{\text{n-sp}}$
A118 $\frac{\text{ho-ba} \cdot 100}{\text{pm-ba}}$
A119 $\frac{\text{s-ba} \cdot 100}{\text{n-s}}$

A120 $\frac{\text{pm-ba} \cdot 100}{\text{ho} \perp \text{pm-ba}}$
A121 pm-ho
A122 ba-ho
A123 ho ⊥ pm-ba pm-ba ‡
A124 ss-n-ba
A125 pm-ho-ba
A127 s-ho
A128 Body height

100	101	102	103	104	105	106	107	108	109	110	111	113	114	115	116	117	118	119	120	121	122	123	124	125	127	128
	.24	.24	.30			.34	.32							–.26			.23			.22			.27			
		.21	.23			.35	.33		.22		–.31	.28	.33	.31		–.22	.23						.29	.23		
																			.22							
									.23																	
			.20						.20	.21															.33	
			.22			.28	.29				.23	.26														
												.35														
																						.24	.22			
	.32	26	.31			.30	.25																			
												.33														
																						.36				

s-n-ss, s-n-sm and ss-n-ba (A102, A103 and A124 respectively) the angles between the mandibular line and the nasion-sella and nasal lines (A106 and A107 respectively), sagittal depth of bony nasopharynx (A109 A125 and A118), indexes for face width/face height (A111 A113), the index for cranial base depth face height (A114), and the indexes for face depth face height and face depth/anterior upper face height (A115 and A117 respectively).

Summary

The significant correlations in Table 27 confirm the assumption that enlarged adenoids on the posterior wall of the nasopharynx and obstructed nose breathing as a consequence of this are common in children with a particular type of facial skeleton. The relationships indicate that individuals who undergo adenoidectomy for obstructed nose breathing frequently display large face height, large height of upper and lower lips, a tendency to small values for the angles s-n-ss and s-n-sm, large angles between the mandibular line and the nasion-sella and nasal lines, small sagittal depth of the bony nasopharynx, and small indexes for face width/face height, cranial base depth/face height and face depth/face height.

Adenoid variables correlated with variables for tongue position

Table 28 shows significant correlations between adenoid variables and variables for tongue position. Variables A34–36 and A38–41 are not included as they correlate strongly (>0 85) with variables A33 A32, A27 A29 A30 A26 and A27 respectively

All the variables for preoperative size of adenoids (A20 A26 A29 and A32) are significantly correlated with the variables for the shortest distances between the tongue and the

Table 27 *Correlations between adenoid variables and variables for the skeleton and lips*

The table only shows correlation coefficients that are significant at the 1 % level (≥0.20)

A80 Face width
A82 Nose width over alae nasi
A83 Nose width above alae nasi
A84 Height of upper lip
A85 n–s
A86 s–ba
A87 n–ba
A88 n–gn
A89 n–sp

A90 sp–gn
A91 ss pm
A92 pm–ba
A93 ho ⊥ pm–ba
A94 s–pm
A95 s ⊥ pm–ba
A96 Height of upper lip
A97 Height of lower lip
A99 lo–lo

A100 bch–bch
A101 bch–bch / pm–ba ho ⊥ pm–ba
A102 s–n–ss
A103 s n–sm
A104 s–n–ss > 82
A105 ss–n–sm
A106 ML/NSL
A107 ML/NL

Variable	A	80	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	99
Ad size before adenoidectomy	20											–.23	–.30		–.22				
Ad. size after adenoidectomy	21																		
Indication for adenoidectomy: obstr nose breathing	22								.32		.25						.21	.24	
Indication for adenoidectomy: recurrent infection	23																		
Indication for adenoidectomy: recurrent otitis media	24															.20			
Indication for adenoidectomy: allergy	25												.21						
ad_1–ba preop.	26													–.21					
ad ba postop.	27												.38						
ad_1–ba difference	28																		
ad_2–ho preop.	29								.21								.20		
ad_2–ho postop	30																		
ad_2–ho difference	31		–.30																
$\frac{\text{Ad. area}\ 100}{\text{pm–ho–ba–pm}}$ preop	32												.22		–.24				
$\frac{\text{Ad. area}\ 100}{\text{pm–ho–ba–pm}}$ postop	33																		
$\frac{\text{Ad area}\ 100}{\text{pm–ho–ba ho' pm}}$ difference	37		–.35											.33					

Adenoid variables correlated with skeleton and lip variables

Significant correlations between adenoid variables and variables for the facial skeleton and lips are shown in Table 27 Variables A81 A98 A112 A126 A34 A35 A36 A38 A39 *A40 and A41* are not included as they correlate very strongly ($r \geq 0.85$) with variables A88 A99 A113 A87 A33 A32, A27 A29 A30 A26 and A27 respectively

There is a large number of significant correlations ($P < 0.01$)

Particularly noteworthy are the significant correlations between skeleton and lip variables and the adenoid variables A20 A32 and A22 i e preoperative size of adenoids in relation to the bony nasopharynx as assessed and measured on radiographs and obstructed nose breathing as an indication for adenoidectomy respectively

Variables A20 and A32 are significantly correlated with variables that express the sagittal depth and volume of the bony nasopharynx (A92 A118 and A101 respectively) posterior upper face height (A94) the angles s–n–ss and s–n–sm (A102 and A103 respectively) the angle ss–n–ba (A124) and the angles between *the mandibular line and the nasion-sella* and nasal lines (A106 and A107 respectively) Large adenoids in relation to the bony nasopharynx are thus frequent among children with a small nasopharynx low posterior upper face height a tendency to small values for the angles s–n–ss and s–n–sm and large angles between the mandibular line and the nasion sella and nasal lines

Obstructed nose breathing as an indication for adenoidectomy (A22) is significantly correlated with total face height (A88) lower face height *(A90) height of upper and lower lips* (A96 and A97 respectively) size of the angles

A108 NL/NSL
A109 ba–s–pm
A110 n–s–ba
A111 $\frac{\text{Face width} \cdot 100}{\text{Face height}}$
A113 $\frac{\text{lo–lo} \cdot 100}{\text{n–gn}}$
A114 $\frac{\text{n–s} \cdot 100}{\text{n–gn}}$
A115 $\frac{\text{ss–pm} \cdot 100}{\text{n–gn}}$
A116 $\frac{\text{n–sp}' \cdot 100}{\text{n–gn}}$
A117 $\frac{\text{ss}'\text{–pm} \cdot 100}{\text{n–sp}}$
A118 $\frac{\text{ho–ba} \cdot 100}{\text{pm–ba}}$
A119 $\frac{\text{s–ba} \cdot 100}{\text{n–s}}$
A120 $\frac{\text{pm–ba} \cdot 100}{\text{ho} \perp \text{pm–ba}}$
A121 pm–ho
A122 ba–ho
A123 ho ⊥ pm–ba pm–ba ½
A124 ss–n–ba
A125 pm–ho–ba
A127 s–ho
A128 Body height

100	101	102	103	104	105	106	107	108	109	110	111	113	114	115	116	117	118	119	120	121	122	123	124	125	127	128
	.24	.24	.30			.34	.32							.26			.23			−.22			.27			
		.21	.23			.35	.33		.22		.31	.28	.33	.31		.22	.23						−.29	.23		
									.23										.22							
			.20						.20	.21															.33	
			.22			.28	.29				.25	.26														
												.35														
.27	.32	.26	.31			.30	.25															−.24	.22			
												.33														
																						.36				

s–n–ss, s–n–sm and ss–n–ba (A102, A103 and A124 respectively), the angles between the mandibular line and the nasion-sella and nasal lines (A106 and A107 respectively), sagittal depth of bony nasopharynx (A109 A125 and A118), indexes for face width/face height (A111 A113) the index for cranial base depth face height (A114) and the indexes for face depth face height and face depth/anterior upper face height (A115 and A117 respectively)

Summary

The significant correlations in Table 27 confirm the assumption that enlarged adenoids on the posterior wall of the nasopharynx and obstructed nose breathing as a consequence of this are common in children with a particular type of facial skeleton. The relationships indicate that individuals who undergo adenoidectomy for obstructed nose breathing frequently display large face height, large height of upper and lower lips, a tendency to small values for the angles s–n–ss and s–n–sm, large angles between the mandibular line and the nasion-sella and nasal lines, small sagittal depth of the bony nasopharynx, and small indexes for face width/face height, cranial base depth/face height and face depth/face height.

Adenoid variables correlated with variables for tongue position

Table 28 shows significant correlations between adenoid variables and variables for tongue position. Variables A34–36 and A38–41 are not included as they correlate strongly ($r \geq 0.85$) with variables A33 A32, A27 A29 A30 A26 and A27 respectively

All the variables for preoperative size of adenoids (A20, A26, A29 and A32) are significantly correlated with the variables for the shortest distances between the tongue and the

Table 28 *Correlations between adenoid variables and variables for tongue position*
The table only shows correlation coefficients that are significant at the 1 % level (≥0.36)

Variable	A	pm–t preop. rest position 129	ba–t_1 preop. rest position 130	$\frac{\text{pm–v}}{2}$–t preop. rest position 131
Ad. size before adenoidectomy	20	45		46
Ad size after adenoidectomy	21			
Indication for adenoidectomy: obstr nose breathing	22	48		45
Indication for adenoidectomy: recurrent infection	23			
Indication for adenoidectomy: recurrent otitis media	24	44		.50
Indication for adenoidectomy: allergy	25			
ad_1–ba preop.	26	46		45
ad_1–ba postop	27			
ad –ba difference	28			
ad_2–ho preop.	29	43		47
ad_2–ho postop	30			
ad_2–ho difference	31			
$\frac{\text{Ad. area} \quad 100}{\text{pm–ho–ba pm}}$ preop	32	43		45
$\frac{\text{Ad. area} \quad 100}{\text{pm ho–ba–pm}}$ postop	33			
$\frac{\text{Ad. area} \quad 100}{\text{pm–ho–ba–ho'–pm}}$ difference	37			

hard and soft palates respectively as measured on lateral cephalometric radiographs (A129 and A131 respectively)

Obstructed nose breathing and recurrent otitis media as indications for adenoidectomy (A22 and A24 respectively) also display significant correlations with the variables for tongue position (A129 A131)

Summary

The significant correlations in Table 28 indicate that a low tongue position is encountered frequently in children with enlarged adenoids and, as a consequence of this obstructed nose breathing or recurrent otitis media

Correlations between airflow variables

Table 29 presents simple correlations between pairs of variables for nasal airflow measured in lit/min at a differential pressure of 10 mm H_2O before and after nose drops on two occasions at an interval of one month All the correlation coefficients are significant at the 0 1 %

Table 30 *Correlations between airflow variables and variables for the skeleton and lips*
The table only shows correlation coefficients that are significant at the 1 level (≥0.20)

A80 Face width
A82 Nose width over alae nasi
A83 Nose width above alae nasi
A84 Height of upper lip
A85 n–s
A86 s–ba
A87 n–ba
A88 n–gn
A89 n–sp
A90 sp –gn
A91 as –pm
A92 pm–ba
A93 ho ⊥ pm–ba
A94 s pm
A95 s ⊥ pm–ba
A96 Height of upper lip
A97 Height of lower lip
A99 lo–lo
A100 bch–bch
A101 bch–bch ho ⊥ pm–ba / pm–ba
A102 s–n–ss
A103 s–n sm
A104 s–n–ss > 82°
A105 ss n–sm
A106 ML/NSL
A107 ML/NL

Variable	A	80	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	99
Preop. airflow before nose drops	67											.4	.37						
Preop. airflow after nose drops	70	.34						.23				.33	30		.31				
Postop. airflow before nose drops	73																		
Postop. airflow after nose drops	76	.29	.25				.25	.25				.34	.27		.27				

Table 29 *Correlations between pairs of airflow variables*

All the correlation coefficients are significant at the 0 1 ‰ level (≥0.27)

Variable	A	67	70	73	76
Preop airflow before nose drops	67				
Preop. airflow after nose drops	70	.55			
Postop. airflow before nose drops	73	.62	.35		
Postop. airflow after nose drops	76	.39	.69	.49	

level. Adenoidectomy was performed on half of the children in the present investigation between the first and second examinations.

Table 29 shows very high significant correlations ($r > 0.62$) for nasal airflow between the first and second examinations before (A67 A73) as well as after (A70, A76) nose drops.

Summary

Table 29 shows high correlations for nasal air flow between the first and second examinations in spite of the fact that half the children underwent adenoidectomy in the interval.

Airflow variables correlated with skeleton and lip variables

Significant correlations between variables for nasal airflow—measured in lit/min at a differential pressure of 10 mm H_2O before and after nose drops on two occasions at an interval of one month—and variables for the facial skeleton and lips are presented in Table 30. Half of the children underwent adenoidectomy in the interval between the first and second examinations. Variables A81 A98, A112 and A126 are not included as they correlate very strongly ($r \geq 0.85$) with variables A88 A99 A113 and A87 respectively

The values for nasal airflow before the administration of nose drops (A67 A73) are to be regarded as measures of the functional air flow while the corresponding values after nose drops (A70, A76) serve as measures of airflow that is more determined by anatomical conditions.

There is a large number of significant correlations ($P < 0.01$) Since airflow after nose drops is determined by anatomical conditions *to a greater* extent than airflow before nose drops, the present account will be confined to correlations between airflow after nose drops at the first and second examinations (A70, A76) on the one hand and skeletal variables on the other

These airflow variables (A70 and A76) are significantly correlated with variables for face

A108 NL/NSL
A109 ba–s–pm
A110 n–s–ba
A111 Face width 100 / Face height
A113 lo–lo 100 / n–gn
A114 n– 100 / gn
A115 n– pm 100 / n–gn
A116 n–sp 100 / n–gn
A117 n– pm 100 / n–sp
A118 ho–ba 100 / pm–ba
A119 s–ba 100 / n–s
A120 pm–ba 100 / ho ⊥ pm–ba
A121 pm–ho
A122 ba–ho
A123 ho ⊥ pm–ba pm–ba ½
A124 s–n–ba
A125 pm–ho–ba
A127 s–ho
A128 Body height

100	101	102	103	104	105	106	107	108	109	110	111	113	114	115	116	117	118	119	120	121	122	123	124	125	127	128
		.22	.24	-.4					.28																	
.3	.3.	.28	.34			.36	.31										.34			.33			.31	.25		
.25		.27	.25	.26																		.29	.26			
.34	.37	.27	.33	-.1		-.4											.24			.26						
																						.29				.27

Table 31 *Correlations between pairs of variables for the skeleton and lips*

The table only shows correlation coefficients that are significant at the 1 ‰ level ($r \geq 0.20$)

Variable	A	80	82	83	84	85	86	87	88	89	90	91	9	93	94	95	96	97	99
Face width	80																		
Nose width over alae nasii	82	.39																	
Nose width above alae nasii	83	31	67																
Height of upper lip	84	.25	.27	.26															
n–s	85	.29	.26		.31														
s–ba	86	40	.26	.20	.37	.29													
n–ba	87	42	.28		.37	.80	69												
n–gn	88	45	.37	.25	49	.33	.54	49											
n–sp	89	42	.28		.31	42	44	.54	79										
sp–gn	90	.28	.23		.39		.37	.26	73	.38									
ss–pm	91	.36	41	.26	.30	.53	.32	.57	.35	.38									
pm–ba	92	.24	.22			.53	43	72				.36							
ho ⊥ pm–ba	93	.22	'20	.29	.22		62	.24	.50	41	.37								
s–pm	94	44	41	43	.38	41	64	45	.57	47	42	.35	.31	61					
s ⊥ pm–ba	95		.21		.21		40	.22	.32	.28	.2.			.29	.31				
Height of upper lip	96	.34	.25	.25	.59		.32	.27	61	.31	.52			.29	.35	.22			
Height of lower lip	97	.23	.30	.25	.31	.20	.35	.25	69	44	.56			.33	45	..4	42		
lo–lo	99	72	.31			.28	.26	.33	.32	.25	.25	.24			.28	.21	.30		
bch–bch	100	43	.34	.33	.28		.27	.22	.38	.30	.30	.31		.24	43		.20	.25	40
bch–bch ho ⊥ pm–ba × pm–ba ⅟	101	46	.39	40	.34	.35	71	.56	.52	43	.38	40	.37	72	74	.30	.30	.36	.35
s–n–ss	102		.23	.26					–.21	–.37		.34	.28		.36				
s–n–sm	103			.25						–.30		.20	.23		.39				
s–n–ss > 82°	104		.25	.27						.29		..5	.23		.35				
ss–n–sm	105																		
ML/NSL	106	–.25																.27	
ML/NL	107	–.23				–.21		–.20	.34		.39	..6	.29	.22			.31	.29	
NL/NSL	108			–.26						.36									
ba–s–pm	109				–.21		–.32		–45	–.34	–.38		64	–64	–43	–31	.26	.31	
n–s–ba	110			–.30			.22	.21					.30	–49	–.51	–.20		.23	
Face width 100 / Face height	111				–.39		–.34	–.25	–74	–.50	–.57			–40	.36		45	.59	
lo–lo 100 / n–gn	113				.33		–.38	–.29	–.81	–64	–.56			–.39	.38		–.39	61	.27
n–s 100 / n–gn	114	–.20			–.27	.38	–.30		72	–45	–.59		.32	–.35	.24	–.23	47	.54	
ss–pm 100 / n–gn	115				–.20		–.23		63	–42	–.50	–.50	.24	.32	–.23		40	.48	
n–sp 100 / n–gn	116				.20					46	–42						37	.28	
ss pm 100 / n–sp	117								50	67	.22	4	.22	.27				.34	
ho–ba 100 / pm–ba	118						.38		.24		.20		30	67					
s–ba 100 / n–s	119	.21				–.31	81		.34		.27			56	.39	.29	.20	..3	
pm–ba 100 / ho ⊥ pm–ba	120						–..4		30	–.25	–.23		34	61	–31	.53		.23	
pm–ho	121	.29	.28	.23		.35	.32	41	.28	.30		34	49		.56		...	.25	
ba ho	122					.31	61	.57	.30	.25		.22	46	44	.29	.25		.22	
ho ⊥ pm–ba pm–ba ⅟	123	33	.30	30	.29	41	80	63	47	40	.3	35	49	.81	71	74	.27	.34	
ss–n ba	124								.34	40	.20	.36	44	.30					
pm–ho–ba	125						–.22		.35	.29	.29		.59	.80	34			.22	
s–ho	127	41	.27	.20	34	.22	68	43	49	37	.37	.22	.28		67	44	.31	.37	.30
Body height	1.8	.56	.35	.28	.34	40	49	.52	67	66	40	48		.36	.53		.35	.35	40

width (A80) face depth (A91) cranial base depth (A87) volume area of cross-section and sagittal depth of bony nasopharynx (A101 A123 and A92 respectively) posterior upper face height (A94) width of posterior choanal aperture (A100) size of the angles s–n–ss and

	100	101	102	103	104	105	106	107	108	109	110	111	113	114	115	116	117	118	119	120	121	122	123	124	125	127	12
3																											
1																											
3	70																										
		.27																									
	23	.28	78																								
		.26	.80	.66																							
			.48		.33																						
			.40	.54	.29																						
		.23		.28		.21	.84																				
			42	.36	41		.26																				
)	25	.28						.32																			
		.27	.40		.42				41	.64																	
		.30		.23			.51	.50		.38																	
		27					.51	41		.35		.84															
,	21	.22					.49	.48		.55		.60	.66														
			.49	33	.37	.29	.53	.51		43		.56	.60	71													
			.28	24	.26			.50	.38		.25	.24			.25												
			.44	46	51	37	.40		.36	.35		.37	.50	.50	.81	.35											
		33						.22		.50	.27	.26	.25	.25	.26												
		50		.20						45	22		.29	.52	.31			44									
		.33						.23		.61	41		.20	.28	.29		.25	42	.25								
		40	-.4	.22	.23													.33									
		53										.22	.28					.54	.40		.39						
	25		.25	.22	.24				.21		.26	.37	.33					.40	.55		.44	.65					
			.76	.55	.37	.42	.33	.23		.49		.29	.31	.29	.42		.68	.44			-.4						
							.25	.36		.82	.55	.36	.31	42	.34		.29	.62	.34					43			
	33			-.4					.23	.37	.30	.27	.37	.31	.25				.52		.33						
	90	.55				.30		.22		.25		.31	42	.29							.29		42				49

s-n-sm (A10_ and A103 respectively) and the angle between the mandibular and nasion-sella lines (A106).

Since variable A76 expresses airflow after adenoidectomy it is also interesting to note the significant correlations between this and

Table 31 *Correlations between pairs of variables for the skeleton and lips*

The table only shows correlation coefficients that are significant at the 1 % level (≥0.20)

Variable	A	80	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	99
Face width	80																		
Nose width over alae nasii	82	39																	
Nose width above alae nasii	83	.31	67																
Height of upper lip	84	.25	.27	.26															
n–s	85	.29	.26		.31														
s–ba	86	40	.26	.20	.37	.29													
n–ba	87	42	.28		.37	.80	69												
n–gn	88	45	.37	.25	49	.33	.54	49											
n–sp	89	42	.28		.31	42	44	.54	79										
sp–gn	90	.28	.23		.39		.37	.26	73	.38									
ss–pm	91	.36	41	.26	.30	.53	.32	.57	35	.38									
pm–ba	92	.24	.22			.53	43	72				.36							
ho ⊥ pm–ba	93	.22	'20	.29	.22		62	.24	.50	41	.37								
s–pm	94	44	41	43	.38	41	64	45	.57	47	42	.35	.31	61					
s ⊥ pm–ba	95		.21		.21		40	.22	.32	.28	.22			.29	.31				
Height of upper lip	96	.34	.25	.25	.59		.32	.–7	61	.31	.52			.29	.35	.22			
Height of lower lip	97	.23	.30	.25	.31	.20	.35	.25	69	44	.56			.33	45	.24	42		
lo–lo	99	72	.31			.28	.26	.33	.32	.25	.25	.24			.28	.21	.30		
bch–bch	*100*	43	.34	.33	.28		.27	.22	.38	.30	.30	.31		.24	43		.20	.25	40
bch–bch ho ⊥ pm–ba pm–ba ‡	101	46	.39	40	.34	.35	71	.56	.52	43	.38	40	.37	72	74	.30	.30	.36	.33
s–n–ss	102		.23	.26					–.21	–.37		.34	.28		.36				
s–n–sm	103			.25						–.30		.20	.23		.39				
s–n–ss > 87°	104		.25	.27						–.29		.28	.23		.35				
ss–n–sm	105																		
ML/NSL	106	–.–5																.27	
ML/NL	107	–.23				.21		–.20	34		.39	.26	–.29	.22			.31	.29	
NL/NSL	108			–.26						.36									
ba–s–pm	109				–.21		–.32		–.45	–.34	–.38		64	–64	–43	–.31	–.26	.31	
n–s ba	110			–.30			.22	.21					.30	–49	–.51	–.20		.23	
Face width 100 / Face height	111				–.39		–.34	–.25	74	–.50	–.57			–40	.36		45	.59	
lo–lo 100 / n–gn	113				.33		–.38	–.29	–.81	–64	–.56			–.39	–.38		.39	61	.27
n–s 100 / n–gn	114	–.20			–.27	.38	–.30		–.7?	–45	–.59		.32	.35	–.–4	–.–3	47	–.54	
ss pm 100 / n–gn	115				–.20		–.23		–63	–42	–.50	–.50	.24	–.32	–.23		40	.48	
n–sp 100 / n–gn	116				.20					46	–42						.37	–.28	
ss pm 100 / n–sp	117								.50	67	–.22	42	.22	–.27				.34	
ho–ba 100 / pm–ba	118						.38		.–4		.20		–.30	67					
s–ba 100 / n–s	119	.21				–.31	81		.34		.27			.56	.39	.29	.20	.23	
pm–ba 100 / ho ⊥ pm–ba	120						–.24		–.30	.25	–.23		34	61	–.31	–.53		.23	
pm–ho	121	.29	.28	.23		35	.32	41	.28	.30		.34	49		.56		.22	.–5	
ba–ho	122					.31	61	57	.30	.25		.–2	46	44	.29	.–5		.22	
ho ⊥ pm–ba pm–ba ‡	123	.33	.30	30	.29	41	80	63	47	40	.32	.35	49	.81	71	74	.–7	.34	
ss–n ba	124								–.34	40	.20	36	44	30					
pm–ho–ba	125						–.–2		–.35	.29	.29		.59	–.80	–.34			.22	
s–ho	1?7	41	.27	.20	34	.22	68	43	49	.37	37	.22	.28		67	44	.31	.37	10
Body height	128	.56	.35	.28	.34	40	49	.52	67	66	40	48		.36	.53		.35	.35	40

width (A80) face depth (A91) cranial base depth (A87) volume area of cross-section and sagittal depth of bony nasopharynx (A101 A123 and A92 respectively) posterior upper face height (A94) width of posterior choanal aperture (A100) size of the angles s–n–ss and

	100	101	102	103	104	105	106	107	108	109	110	111	113	114	115	116	117	118	119	120	121	122	123	124	125	127	128
	.70																										
		.27																									
	.23	.28	.71																								
		.26	.80	.66																							
			.48		.33																						
			.40	.54	.29																						
		.23		.28		.21	.84																				
			.42	.36	.41		.26																				
	.25	.28						.32																			
		.27	.40		.42				.41	.64																	
		.30		.23			.51	.50		.58																	
		.27					.51	.41		.35		.84															
	.21	.22					.49	.48		.55		.60	.66														
			.49	.33	.37	.29	.53	.51		.43		.56	.60	.71													
			.28	.24	.26			.50	.38		.23	.24			.25												
			.64	.46	.31	.37	.40		.36	.35		.37	.50	.50	.81	.35											
		.33						.22		.50	.27	.26	.25	.25	.26												
		.50		.20						.43	.22		.29	.52	.31			.44									
		.33						.23		.61	.41		.20	.28	.29		.25	.42	.25								
		.40	.24	.22	.23													.33									
		.53										.22	.28					.54	.40		.39						
	.25		.25	.22	.24				.21		.26	.32	.33					.40	.55		.44	.65					
			.76	.55	.57	.42	.33	.23		.49		.29	.31	.29	.62		.68	.44			.24						
							.25	.36		.82	.55	.36	.31	.43	.34		.29	.62	.34					.43			
	.33			.24					.23	.37	.30	.27	.32	.31	.25				.52		.33						
	.90	.55				.50		.22		.25		.31	.42	.29							.29		.42			.49	

t-n-sm (A102 and A103 respectively) and the angle between the mandibular and nasion-sella lines (A106)

Since variable A76 expresses airflow after adenoidectomy it is also interesting to note the significant correlations between this and

Table 31 *Correlations between pairs of variables for the skeleton and lips*

The table only shows correlation coefficients that are significant at the 1 % level (≥0.20)

Variable	A	80	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	99
Face width	80																		
Nose width over alae nasi	82	.39																	
Nose width above alae nasi	83	.31	67																
Height of upper lip	84	.25	.27	.26															
n–s	85	.29	.26		.31														
s–ba	86	40	.26	.20	.37	.29													
n–ba	87	42	.28		.37	80	69												
n–gn	88	45	37	.25	49	.33	.54	49											
n–sp	89	42	.28		.31	42	44	.54	79										
sp–gn	90	.28	.23		39		.37	.26	73	.38									
ss'–pm	91	.36	41	.26	.30	.53	.32	.57	.35	.38									
pm–ba	92	.24	.22			.53	43	72				.36							
ho ⊥ pm–ba	93	.22	20	.29	.22		.62	.24	.50	41	.37								
s–pm	94	44	41	43	.38	41	64	45	.57	47	42	.35	31	61					
s ⊥ pm–ba	95		.21		.21		40	.22	32	.28	.22			.29	31				
Height of upper lip	96	.34	.25	.25	.59		.32	.27	61	.31	.52			.29	.35	.22			
Height of lower lip	97	.23	.30	.25	.31	.20	.35	.25	69	44	.56			.33	45	-.4	42		
lo–lo	99	72	.31			.28	.26	.33	.32	.25	.25	.24			.28	.21	.30		
bch–bch	100	43	.34	.33	.28		.27	.22	.38	.30	.30	.31		.24	43		.20	.25	40
bch–bch × ho ⊥ pm–ba / pm–ba × ½	101	46	.39	40	.34	35	71	.56	52	43	.38	40	.37	72	74	.30	.30	.36	.35
s–n–ss	102		.23	.26					-.21	-.37		.34	.28		.36				
s–n–sm	103			.25						-.30		.20	.23		39				
s–n–ss > 82°	104		.25	.27						.29		.28	.23		.35				
ss–n–sm	105																		
ML/NSL	106	-.25																.27	
ML/NL	107	.23				.21		-.20	.34		.39	-.6	.29	.22			.31	.29	
NL/NSL	108			.26						36									
ba s–pm	109				-.21		-.32		-45	.34	-.38		64	-64	-43	.31	.26	.31	
n–s–ba	110			-.30			.22	.21					.30	49	-.51	.20		.23	
Face width 100 / Face height	111				-.39		-.34	.25	-74	-50	-.57			-40	36		45	.59	
lo–lo 100 / n–gn	113				.33		-.38	.29	81	-64	-.56			-.39	-.38		.39	61	.27
n–s 100 / n–gn	114	-.20			-.27	.38	-30		-72	-45	.59		.32	-.35	-.4	.23	47	-.54	
ss pm 100 / n–gn	115				-.20		-.23		63	-42	-.50	.50	.24	-.32	-.23		40	-.48	
n sp 100 / n–gn	116				.20					46	42						37	-.28	
ss–pm 100 / n–sp	117								50	67	.22	42	.22	.27				.34	
ho–ba 100 / pm–ba	118						.38		.24		.20		30	67					
s–ba 100 / n–s	119	.21				-.31	81		.34		.27			.56	39	.29	.20	.23	
pm–ba 100 / ho ⊥ pm–ba	120						.24		-.30	.25	-.23		.34	61	-31	53		.23	
pm–ho	121	.29	.28	.23		35	32	41	.28	30		.34	49		.56		.22	.25	
ba–ho	122					.31	61	.57	30	.25		.22	46	44	.29	.25		.22	
ho ⊥ pm–ba pm–ba ½	123	.33	30	.30	.29	41	.80	63	47	40	32	.35	49	.81	71	74	.27	.34	
ss–n–ba	124								.34	40	.20	36	44	.30					
pm–ho–ba	125						-.2		-.35	.29	.29		.59	.80	34			.22	
s–ho	127	41	.27	.20	.34	.22	68	43	49	.37	37	.22	.28		67	44	31	.37	.30
Body height	128	.56	.35	.28	.34	40	49	.52	67	66	40	48		36	.53		35	35	40

width (A80) face depth (A91) cranial base depth (A87) volume area of cross-section and sagittal depth of bony nasopharynx (A101 A123 and A92 respectively) posterior upper face height (A94) width of posterior choanal aperture (A100), size of the angles s–n–ss and

8 NL/NSL	A115 $\frac{\text{ss–pm} \quad 100}{\text{s–gn}}$	A120 $\frac{\text{pm–ba} \quad 100}{\text{ho} \perp \text{pm–ba}}$
9 ba–s–pm	A116 $\frac{\text{n–sp} \quad 100}{\text{n–gn}}$	A121 pm–ho
0 n–s–ba	A117 $\frac{\text{ss–pm} \quad 100}{\text{n–sp'}}$	A122 ba–ho
1 $\frac{\text{Face width} \quad 100}{\text{Face height}}$	A118 $\frac{\text{ho–ba} \quad 100}{\text{pm–ba}}$	A123 ho ⊥ pm–ba pm–ba
13 $\frac{\text{lo–lo} \quad 100}{\text{s–gn}}$	A119 $\frac{\text{s–ba} \quad 100}{\text{n–s}}$	A124 ss–n–ba
14 $\frac{\text{n–s} \quad 100}{\text{s–gn}}$		A125 pm–ho–ba
		A127 s–ho
		A128 Body height

0	101	102	103	104	105	106	107	108	109	110	111	113	114	115	116	117	118	119	120	121	122	123	124	125	127	128
						.36					42	.52	.53													47

($r > 0.85$) to variables A88, A99 A113 and A87 respectively

There is a very large number of significant correlations ($P < 0.01$)

Summary

Significant correlations were found between the majority of the skeletal variables shown in Table 31 This applied in particular to variables that express measurements of angles or dimensions in the same projection plane.

Skeleton and lip variables correlated with variables for tongue position

Significant correlations between skeleton and lip variables on the one hand and variables for tongue position on the other are shown in Table 32. Variables A81 A98 A112 and A126 are not included as they correlate very strongly (> 0.85) to variables A88 A99 A113 and A87 respectively

The significant correlations shown in Table 32 chiefly refer to the relationship between, on the one hand, the shortest distance between the tongue and the hard palate along a perpendicular to the nasion–sella line through pterygomaxillare (A129) and, on the other skeleton and lip variables that express face height (A88, A89) height of upper lip (A96) the angle between the mandibular and nasion-sella lines (A106) indexes for face width/face height (A111 A113) and for cranial base depth/face height (A114)

Summary

The significant correlations shown in Table 32 between variables for tongue position and variables for the facial skeleton and lips are in good agreement with the relationships already described between variables for mode of breathing and variables for the facial skeleton and lips (cf. Table 18, p 60)

Thus, it is common for a low tongue position to be found in children with the following skeletal characteristics: large face height, large height of upper lip, large angle between mandibular and nasion-sella lines and small index values for face width/face height and cranial base depth/face height. These skeletal characteristics are the same as those which were shown in Table 12 (p 50) to be characteristic of the children in group 5 i.e. those who underwent adenoidectomy on account of obstructed nose breathing.

Correlations between variables for tongue position

Table 33 presents simple correlations between all pairs of variables for tongue position.

The table shows that the variables for tongue position in relation to the hard and soft palates (A129 and A131 respectively) are strongly intercorrelated ($r = 0.73$)

Table 32. *Correlations between variables for the skeleton and lips and variables for tongue position*
The table only shows correlation coefficients that are significant at the 1 % level ($r \geq 0.20$)

A80 Face width
A82 Nose width over alae nasii
A83 Nose width above alae nasii
A84 Height of upper lip
A85 n–s
A86 s–ba
A87 n–ba
A88 n–gn
A89 n–sp
A90 sp –gn
A91 ss –pm
A92 pm–ba
A93 ho ⊥ pm–ba
A94 s–pm
A95 s ⊥ pm–ba
A96 Height of upper lip
A97 Height of lower lip
A99 lo–lo
A100 bch–bch
A101 bch bch / pm–ba ho ⊥ pm–ba
A102 s–n–ss
A103 s–n–sm
A104 s–n–ss > 82°
A105 ss–n–sm
A106 ML/NSL
A107 ML/NL

Variable	A	80	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	99
pm–t preop. rest position	129								.51	40							40		
ba–t preop. rest position	130																		
$\frac{pm-v}{2}$–t preop rest position	131																		

variables for nose width (A82) the distance from the midpoint of sella turcica to basion (A86) the angle s–n–ss > 82 (A104) and body height (A128)

Thus, a small nasal airflow is recorded frequently among children with a narrow face and nose, short distance between sella turcica and basion short depth of face and cranial base small nasopharynx, small posterior upper face height, narrow posterior choanal aperture, small values for the angle s–n–ss, a large angle between the mandibular and nasion-sella lines and small body height

Summary

The significant correlations shown in Table 30 confirm the hypothesis that there is a relationship between nasal airflow and facial type A small nasal airflow is recorded frequently among children with a narrow face and nose, short distance between sella turcica and basion short depth of face and cranial base, small *nasopharynx low posterior upper face height*, narrow posterior choanal aperture, small values for the angle s–n–ss, a large angle between the mandibular and nasion-sella lines and small body height

Airflow variables correlated with variables for tongue position

No significant correlations were found between the variables for nasal airflow on the one hand and variables for tongue position (A129–131) on the other

Correlations between variables for the facial skeleton and lips

Table 31 presents simple correlations between pairs of variables for the facial skeleton and lips Variables A81 A98, A112 and A126 are not included as they correlate very strongly

Table 33 *Correlations between all pairs of variables for tongue position*
The table only shows correlation coefficients that are significant at the 1 level ($r \geq 0.36$)

Variable	A	129	130	131
pm–t preop. rest position	129			
ba–t_s preop. rest position	130			
$\frac{pm-v}{2}$ t preop rest position	131	73		

A108 NL/NSL
A109 ba–s–pm
A110 n–s–ba
A111 $\frac{\text{Face width} \quad 100}{\text{Face height}}$
A113 $\frac{\text{lo–lo} \quad 100}{\text{n–gn}}$
A114 $\frac{\text{n–s} \quad 100}{\text{n–gn}}$
A115 $\frac{\text{ss–pm} \quad 100}{\text{n–gn}}$
A116 $\frac{\text{n–sp} \quad 100}{\text{n–gn}}$
A117 $\frac{\text{ss'–pm} \quad 100}{\text{n–sp}}$
A118 $\frac{\text{bo–ba} \quad 100}{\text{pm–ba}}$
A119 $\frac{\text{s–ba} \quad 100}{\text{n–s}}$
A120 $\frac{\text{pm–ba} \quad 100}{\text{bo} \perp \text{pm–ba}}$
A121 pm–bo
A122 ba–bo
A123 bo ⊥ pm–ba pm–ba ‡
A124 ss–n–ba
A125 pm–bo–ba
A127 s–bo
A128 Body height

100	101	102	103	104	105	106	107	108	109	110	111	113	114	115	116	117	118	119	120	121	122	123	124	125	127	128
						.36					–.42	.52	.53													.47

($r \geq 0.85$) to variables A88 A99 A113 and A87 respectively

There is a very large number of significant correlations ($P < 0.01$)

Summary

Significant correlations were found between the majority of the skeletal variables shown in Table 31 This applied *in particular* to variables that express measurements of angles or dimensions in the same projection plane.

Skeleton and lip variables correlated with variables for tongue position

Significant correlations between skeleton and lip variables on the one hand and variables for tongue position on the other are shown in Table 32. Variables A81 A98 A112 and A126 are not included as they correlate very strongly ($r > 0.85$) to variables A88, A99 A113 and A87 respectively

The significant correlations shown in Table 3 *chiefly refer* to the relationship between, on the one hand, the shortest distance between the tongue and the hard palate along a perpendicular to the nasion-sella line through pterygomaxillare (A129) and, on the other skeleton and lip variables *that express face height* (A88, A89), height of upper lip (A96), the angle between the mandibular and nasion-sella lines (A106), indexes for face width/face height (A111 A113) and for cranial base depth/face height (A114)

Summary

The significant correlations shown in Table 32 between variables for tongue position and variables for the facial skeleton and lips are in good agreement with the relationships already described between variables for mode of breathing and variables for the facial skeleton and lips (cf. Table 18 p 60)

Thus, it is common for a low tongue position to be found in children with the following skeletal characteristics: large face height, large height of upper lip, large angle between mandibular and nasion-sella lines and small index values for *face width/face height* and cranial base depth/face height. These skeletal characteristics are the same as those which were shown in Table 12 (p 50) to be characteristic of the children in group 5 i.e. those who underwent adenoidectomy on account of obstructed nose breathing.

Correlations between variables for tongue position

Table 33 presents simple correlations between all pairs of variables for tongue *position*.

The table shows that the variables for tongue position *in relation to the hard and soft palates* (A129 and A131 respectively) are strongly intercorrelated ($r = 0.73$)

Results and discussion of multiple regression analyses

CHOICE OF REGRESSANDS

The regressand chosen in order to study which factors influence the mode of breathing is the alternative variable A15 i.e mouth breathing (yes/no) This variable was preferred to the other mode of breathing variables (A04 A05 and A12) since it was registered by the same observer in all the children

The regressands chosen to investigate which factors influence nasal airflow before adenoidectomy are the variables for preoperative nasal airflow before (A67) and after (A70) nose drops The simple correlation analysis has shown that there are strong intercorrelations between the variables for nasal airflow measured at differential pressures of 10 15 and 20 mm H_2O ($r > 0.97$) before nose drops and consequently that airflow measured at 10 mm H_2O (A67) is fully representative of airflow at 15 and 20 mm H_2O This also applies to the airflow measurements after nose drops. The measurements at 10 mm H_2O have been chosen because they were obtained in more children than at 15 and 20 mm H_2O owing to the fact that so many of the children had nasal obstructions.

In order to study whether the importance of the regressors for airflow is changed by the administration of nose drops, a separate analysis has been performed with the same regressors as above but with the intraindividual difference between variables A70 and A67 as the regressand (p 90)

Different combinations of groups of variables have been analyzed in order to study how different groups of variables determine the variation in nasal airflow before as well as after adenoidectomy (p 91)

The regressands selected for the analysis of dentition variables are the angle between the upper incisors and the nasion-sella line (A46), the angle between the lower incisors and the mandibular line (A48) upper arch width between first molars (A49) overjet (A55) overbite (A56) sagittal relation between upper and lower first molars on right and left (A57 and A58 respectively) the relationship between lower and upper arch width between first molars (A63) and the relationship between height of palatal vault and upper arch width between first molars (A66) These variables were chosen on account of their relationships with the nasal airway variables represented by the anamnesis, adenoid and airflow variables (see Tables 15 21 and 22, pp 56, 64 and 65 respectively) The dentition variables (A46 A48 A49 and A63) were also chosen as regressands on account of the significant differences obtained for them in comparisons between the means for control group 1 and group 5 adenoidectomy for obstructed nose breathing (see Table 9 p 41)

The skeleton variable A107 Angle between the mandibular and nasal lines, has been chosen as a regressand on the same grounds as for the dentition variables above

NUMBER OF CHILDREN INCLUDED FOR THE REGRESSANDS

The number of children included in each multiple regression analysis has been limited to the number for whom values were obtained for the regressand in question In the case of the airflow variables, for instance measurements were not obtained in approximately

15% of the 162 children consequently their values for the regressors were also excluded in the analyses with an airflow variable as regressand.

CHOICE OF REGRESSORS

The regressors chosen for the multiple regression analyses are those listed in Table 1 (pp 13–15) with the following exceptions.

(*a*) Variables which are closely related to the regressand, e.g. when the regressand was A15 Mouth breathing, the variable for mouth in sleep (A05) was not included.

(*b*) Variables that could not be registered in a large number of children.

(*c*) Variables for which a causal influence from the regressand is suspected. For this reason, variables based on information one month after adenoidectomy are with some exceptions excluded if the regressand refers to conditions before adenoidectomy (e.g. A67 A73).

(*d*) If several variables display very high intercorrelations, one of them has been selected to represent the others. A67 for instance, represents A68 and A69

(*e*) Variables have often been excluded if the simple correlation analysis shows that the correlation to the regressand do not reach the 1% level of significance.

SUBSTITUTION OF MISSING VALUES FOR REGRESSORS

In the multiple regression analyses, missing values have been replaced by the mean for the regressor in question

PRINCIPLES FOR THE PRESENTATION OF MULTIPLE REGRESSION ANALYSES

A specified list of the variables concerned is given in the account of each regression analysis. Stepwise regression analysis was performed and the tables only show the variables which are significant at the 5% level. The regression tables also list the regression coefficients and their standard error *t*-values, the partial correlations between the regressand and each of the regressors with allowance made for the other regressors in the table, the total correlation or coefficient of determination (R^2) and the standard deviation of the residuals (R.S.D.)

The multiple regression analyses in this study concern all the children for which each regressand has been registered, at most 162 individuals (see Tables 7 9 11 and 12, pp 38 41 47 and 50 respectively)

One analysis has been made, however on the adenoidectomy children alone See p 84

REGRESSAND MOUTH BREATHING

In the analysis presented in Table 34 the regressand was variable A15 Mouth breathing, and the regressors were as follows. anamnesis variables A02–03 A16 adenoid variables A26 A29–30 A32–36, A38–41 dentition variables A49 A55 A60 airflow variables A67 A70 and skeleton variables A80 A82–83 A87–95 A100–102, A104–106 A109–110 A112–118 A121–126 (for definitions see Table 1 pp 13–15) The regressors which proved to be significant at the 5% level were introduced in the following order A16, A40, A41 A109 A83 A55

Results

According to this regression analysis, the clinical assessment of enlarged adenoids (A16) and the preoperative size of adenoids in relation to sagittal depth of the bony nasopharynx (A40) are the two most important determinants of mouth breathing.

The coefficient of determination for the regressors included ($R^2 = 0.74$) is entirely satisfactory

The variables having regression coefficients which are highly significant ($P < 0.001$) have the expected sign.

CHAPTER 7

Results and discussion of multiple regression analyses

CHOICE OF REGRESSANDS

The regressand chosen in order to study which factors influence the mode of breathing is the alternative variable A15 i.e. mouth breathing (yes/no) This variable was preferred to the other mode of breathing variables (A04 A05 and A12) since it was registered by the same observer in all the children

The regressands chosen to investigate which factors influence nasal airflow before adenoidectomy are the variables for preoperative nasal airflow before (A67) and after (A70) nose drops The simple correlation analysis has shown that there are strong intercorrelations between the variables for nasal airflow measured at differential pressures of 10 15 and 20 mm H_2O ($r > 0.97$) before nose drops and consequently that airflow measured at 10 mm H_2O (A67) is fully representative of airflow at 15 and 20 mm H_2O This also applies to the airflow measurements after nose drops The measurements at 10 mm H_2O have been chosen because they were obtained in more children than at 15 and 20 mm H_2O owing to the fact that so many of the children had nasal obstructions

In order to study whether the importance of the regressors for airflow is changed by the administration of nose drops, a separate analysis has been performed with the same regressors as above but with the intraindividual difference between variables A70 and A67 as the regressand (p 90)

Different combinations of groups of variables have been analyzed in order to study how different groups of variables determine the variation in nasal airflow before as well as after adenoidectomy (p 91)

The regressands selected for the analysis of dentition variables are the angle between the upper incisors and the nasion sella line (A46), the angle between the lower incisors and the mandibular line (A48) upper arch width between first molars (A49) overjet (A55) over bite (A56) sagittal relation between upper and lower first molars on right and left (A57 and A58 respectively) the relationship between lower and upper arch width between first molars (A63) and the relationship between height of palatal vault and upper arch width between first molars (A66) These variables were chosen on account of their relationships with the nasal airway variables represented by the anamnesis, adenoid and airflow variables (see Tables 15 21 and 22, pp 56 64 and 65 respectively) The dentition variables (A46 A48 A49 and A63) were also chosen as regressands on account of the significant differences obtained for them in comparisons between the means for control group 1 and group 5 adenoidectomy for obstructed nose breathing (see Table 9 p 41)

The skeleton variable A107 Angle between the mandibular and nasal lines has been chosen as a regressand on the same grounds as for the dentition variables above

NUMBER OF CHILDREN INCLUDED FOR THE REGRESSANDS

The number of children included in each multiple regression analysis has been limited to the number for whom values were obtained for the regressand in question In the case of the airflow variables, for instance, measurements were not obtained in approximately

separate regression analysis was made for these two groups using the same set of variables and procedure as in the analysis above.

The results, presented in Table 35 display good agreement with those for the main analysis in Table 34 except that variable A 16, representing the clinical assessment of enlarged adenoids, does not appear because almost all the children in the adenoid groups presented enlarged adenoids The coefficient of determination is thereby markedly reduced to $R^2 = 0.34$

Discussion

Out of a total of 162 children in this study 67 were mouth breathers, 1 belonging to the controls and 66 to the adenoidectomy groups (cf. Table 7 p 38) It should be emphasized, however that two potential control children were transferred to the adenoidectomy groups on account of obstructed nose breathing (see p 12)

It is therefore hardly surprising that variables A16 and A40–41 which represent size of adenoids, constitute the most important group of factors for determining why certain children breath through the mouth and others through the nose

Large adenoids can thus be interpreted as causing mouth breathing. The frequency with which mouth breathing was caused by adenoids in the population is difficult to determine from the present study since there is an overrepresentation of the adenoidectomy groups in relation to the control groups, which comprise only 1% of the population of Örebro Furthermore, children with nasal obstruction have been excluded from the original control material.

Enlarged adenoids are said by Brash (1929) and Nervert (1939) to be the main cause of mouth breathing. Leech (1958) has reported that adenoids caused mouth breathing in 13% of 500 children, of whom 19% were mouth breathers. Reed (1963) has maintained that adenoids is the most common cause of nasopharyngeal obstruction with mouth breathing as a consequence.

The opposite opinion—that nasal obstruction is rarely caused by adenoids—has been voiced by James & Hastings (1932), while Ballard & Gwynne-Evans (1958) have reported that flaccidity of the oropharyngeal musculature or swelling of the anterior nasal mucosa is more frequently responsible for mouth breathing in children than adenoidal enlargement. Steele (1968) also holds that nasal obstruction is not always due to adenoid or tonsil hypertrophy

The variable for swollen nasal mucosa (A18) has not been included among the regressors in the present analysis, which means that any effect on the regressand of such swelling as a consequence of adenoids will have been attributed to the regressors for size of adenoids. At the same time, the simple correlation analysis showed that swollen nasal mucosa is weakly correlated to mouth breathing ($r = 0.19$) Furthermore, the overrepresentation of children with adenoids in the adenoidectomy groups may help to explain why swollen nasal mucosa appears to have so little to do with mouth breathing.

The next most important variable in the regression equation after size of adenoids for determining the mode of breathing is A109 which represents the sagittal depth of the bony nasopharynx. This variable serves to represent the skeleton variables that express various dimensions in the nasopharyngeal region. The observed relationship prompts the conclusion that even children with large adenoids may have an adequate nasal airway if the nasopharynx is large and that consequently such children are not obliged to become mouth breathers. The effect of adenoid size on mode of breathing can thus be judged to be dependent on the size of the nasopharynx. This is also indicated by the relationships represented in Fig. 24 in which zones I and II have been delimited in an approximate way so that the former is dominated by mouth breathers and the latter by nose breathers, while both modes of breathing are represented to the same extent

Table 34 *Regressand. A15 Mouth breathing*

Regression coefficients, their std. error level of significance (marked with asterisks), partial correlation coefficients, the total correlation coefficient (R^2) and the standard deviation of the residuals (R.S.D) in an analysis of 53 regressors

Regressor	Coefficient	Std. error	t-value	Partial corr
Constant	1 6390	0 4153	3.95	—
A16 Enlarged adenoids	0 4444	0 0710	6.26 *	0.45
A40 Preop. size of ad.	0 0156	0.0026	6.06	0.44
A41 Postop size of ad.	−0.0088	0.0025	−3.50	−0.27
A55 Overjet	0.0231	0.0107	2.16	0.17
A83 Nose width	−0 0287	0.0131	−2.19	−0.17
A109 ba–s–pm	−0.0147	0 0041	−3.58	−0.28

$R^2 = 0$ 74 R.S.D −0.25

An interesting finding is that variable A16 by itself has the coefficient of determination $R^2 = 0$ 63 (cf Table 14 p 55) In other words, size of adenoids counts for most of the total coefficient of determination It will also be seen that the clinical assessment of size of adenoids has a little higher correlation to mouth breathing than size of adenoids assessed and measured on lateral cephalometric radiographs.

The variables that are highly significant ($P <$ 0 001) in this regression analysis and which represent size of adenoids (A16 A40–41) dominate the analysis and by themselves have a high coefficient of determination $R^2 = 0$ 70 *The appearance of variable A41 is difficult to* interpret as it represents size of adenoids in relation to sagittal depth of the bony nasopharynx after adenoidectomy whereas the regressand—A15 Mouth breathing—refers to conditions before the operation. A conceivable interpretation is that the more of the adenoids that was removed at adenoidectomy the greater was the previous propensity to breath through the mouth In other words, it is conceivable that adenoidectomy was more radical in children with particularly large adenoids.

Variable A109 which represents sagittal depth of the bony nasopharynx, also appears to play some part in determining mouth breathing since it has a partial correlation coefficient of −0 28

The other variables included in the regression equation are A83 Nose width above alae nasil, and A55 Overjet. Both these are only almost significant ($P < 0$ 05)

Thus, it appears that mouth breathing occurs in the first place frequently in children with large adenoids and a small sagittal depth of nasopharynx.

Since it has been shown that almost all the mouth breathers in the present study belonged to groups 4 and 5 (cf Table 7 p 38), a

Table 35 *Regressand A15 Mouth breathing in an analysis for the children in groups 4 and 5*

Analysis analogous with that reported in Table 34

Regressor	Coefficient	Std. error	t-value	Partial corr
Constant	3.0486	0.7399	4 12	—
A40 Preop size of ad	0 0151	0 0034	4 45	0 45
A82 Nose width	−0.0429	0.0176	−2.44	−0.27
A109 ba–s–pm	−0.0177	0 0063	−2.81	−0.30

$R^2 = 0.34$ R.S.D −0.32

Summary

This multiple regression analysis has shown that mouth breathing occurs frequently in children with large adenoids and a small nasopharynx in the sagittal plane For the children in this study mouth breathing is largely explained as a consequence of the size of adenoids and the size of the bony nasopharynx.

REGRESSAND NASAL AIRFLOW PREOPERATIVELY BEFORE NOSE DROPS

In the analysis presented in Table 36 the regressand was variable A67 Nasal airflow measured before nose drops preoperatively at a differential pressure of 10 mm H_2O and the regressors were as follows. anamnesis variables A02–03 A06, A18 adenoid variables A20, A21 A26, A29 A32, A35 A38 A40 dentition variables A44–49 A51 A53 A55–56, A59–61 A63 A66 skeletal variables A80 A82–83 A87–89 A91–95 A100–103 A106, A109–110, A113 A118, A120–125 (for definitions see Table 1 pp 13–15) The regressors were introduced in the following order A20, A92, A18, A118, A55 A44 A06

Results and discussion

The relationship between the regressand (A67) and the variable for size of adenoids (A20) is also shown diagrammatically in Fig. 25 It will be seen from the figure that nasal airflow is lowest for large adenoids and highest for small or no adenoids A study of the regression lines shows that size of nasopharynx is of little importance for airflow if the adenoids are large or very large The change in airflow with increasing nasopharyngeal space is greatest in the middle group—small or moderate adenoids. The differences between the slopes of these regression lines are almost significant ($P < 0.05$)

A reasonable interpretation of this diagram is that the size of the nasopharynx is of little importance for airflow if the adenoids are large and impede the passage of air If there are no adenoids, airflow is again largely unaffected by the size of the nasopharynx because this does not then greatly determine the passage of air Thus it is only in children with small or moderate adenoids that the size of the nasopharynx is of essential importance for nasal airflow

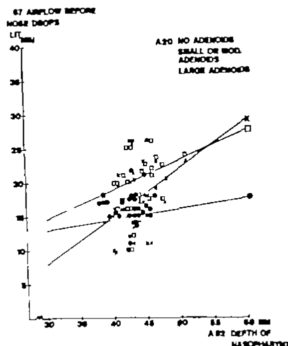


Fig 25 Diagram showing the influence of adenoid size (A20) on the relationship between nasal airflow before nose drops before adenoidectomy (A67) and depth of nasopharynx in the sagittal plane (A92). Adenoid size has been arranged in three groups. 1 no adenoids; 2, small or moderate adenoids; 3 large or very large adenoids. The values of each child are marked by plot.

It will be seen that nasal airflow is lowest for large adenoids and highest for small or no adenoids. A regression line is given for each adenoid group showing the relationship between the regressand airflow (A67) and the regressor depth of nasopharynx in the sagittal plane (A92). The slope and position of the regression lines were determined with the computer The diagram indicates that larger nasopharynx is of little importance for the airflow if the adenoids are large or very large. Airflow changes most with increasing nasopharyngeal space in the middle group—small or moderate adenoids.

The regressors included in the regression equation as determinants of A67 Airflow at a

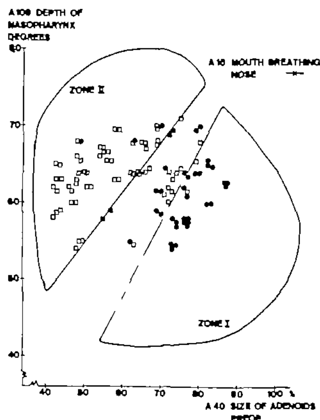


Fig 24 Diagram showing mode of breathing (A15) in relation to size of adenoids (A40) and depth of nasopharynx in the sagittal plane (A109). The values of each child are marked by a plot. Zone I is dominated by mouthbreathers, zone II by nosebreathers both modes of breathing occur to the same extent in the intermediate zone

in the intermediate zone This figure reproduces the primary information presented in the regression table namely that variables A109 and A40 have large determinative values vis-à-vis mouth breathing.

The view that the effect of adenoid size on mode of breathing can be said to be dependent on the size of the nasopharynx has previously been expressed by Bernfeld (1929) Schüller (1929) Emslie, Massler & Zwemer (1952), Ricketts (1954) Goldman & Bachman (1958) and Lubarth (1960)

Of the other regressors in the regression equation (A83 and A55) the variable for nose width above alae nasii (A83) can also be said to represent the size of the nasal airway A causal relationship appears probable between the size of the nasal airway and mode of breathing.

As a regressor in the regression equation, variable A55 Overjet, is to be regarded as representing the variables for dimensional relationships between the upper and lower jaws (see the regression analysis with A55 as regressand p 100) The relationship between variable A55 and mode of breathing can be interpreted in part as a parallel phenomenon to the sagittal relationship between the upper and lower jaws and in part as a causal relationship This means that a large overjet is frequent among children who are mouth breathers It should be noted, however that this *relationship is uncertain as the partial correlation* coefficient is only 0 17 and no more than almost significant ($P < 0\ 05$)

Table 36 *Regressand A67 Nasal airflow at a differential pressure of 10 mm H_2O preoperatively before nose drops*

Regression coefficients, their std error level of significance (marked with asterisks), partial correlation coefficient the total correlation coefficient (R^2) and the standard deviation of the residuals (R.S.D) in an analysis of 5 regressor

Regressor	Coefficient	Std error	t-value	Partial corr
Constant	17.2430	7 9393	2.17	—
A06 Recurrent infect.	1 8194	0.8878	2.05	0.18
A18 Swollen nasal mucosa	−5.5134	1.5886	−3 47	−0.29
A20 Preop size of ad.	−1 7607	0.3547	−4 96	−0.40
A44 OL/ML	0 1938	0 0915	2.12	0 18
A55 Overjet	−0 4623	0.1924	−2.40	0.21
A92 pm–ba	0.4272	0 1197	3.57	0 30
A118 ho–ba/pm–ba	−0.2001	0.0783	−2.56	0.22

$R^2 = 0\ 40$ R.S D = 4.21

Table 37 *Regressand: A70 Nasal airflow at a differential pressure of 10 mm H_2O preoperatively after nose drops*

Analysis analogous with that reported in Table 36

Regressor	Coefficient	Std. error	*t*-value	Partial corr
Constant	−42.9080	17 9360	−2.39	—
A20 Preop. size of ad.	−2.1064	0 4333	−4.86	0.39
A80 Face width	0.3522	0 1317	2.67	0.23
A103 s-n-sm	0.4888	0 1701	2.87	0.24

R^2 0.32; R.S.D 6.00.

Fig. 21 p. 50) The low value of R^2 should be seen in relation to the large error of method for variable A70 This error amounts to 28 % of the variance for all the children in the study (cf. Table 5 p 29), which means that one cannot expect a higher value of R^2 than 0 72 The observed value should therefore be seen in relation to this maximum, i.e. (0.32/0 72) 100 or 44 % as an indication of the determinative value of the regressors in this regression analysis

Size of adenoids as expressed by variable A20 is shown by this analysis to be the most important determinant of airflow at a differential pressure of 10 mm H_2O after nose drops as well. The coefficient of determination with this variable alone amounts to 0.23 The relationship between size of adenoids and nasal airflow is negative (cf. Table 26 p 73) which indicates, as expected, that airflow is low when adenoids are large

The positive relationship between airflow after nose drops (A70) and the degree of prognathism in the lower jaw (A103) can be interpreted as indicating that facial types with little prognathism frequently have a lower nasal airflow It is conceivable, however that this relationship is also influenced by a small posterior upper face height. Evidence to this effect is to be found in the significant positive simple correlation coefficients between variable A70 and the variables for degree of prognathism in the upper (A102) and lower (A103) jaws (r = 0.28 and 0 34 respectively cf Table 30 p 77) This regression analysis thus reveals a relationship between airflow at a differential pressure of 10 mm H_2O after nose drops on the one hand and, on the other the variables that express the degree of prognathism in the upper and lower jaws (A102 and A103 respectively).

The variable for face width (A80) also displays a relationship with airflow after nose drops (A70) This can be interpreted as a consequence of the strongly significant correlations between A80 and the variables for posterior choanal width (A100) and volume of bony nasopharynx (A101), i.e r = 0.43 and 0 46 respectively (cf. Table 31 p 78)

This analysis thus indicates that the regressors included in the regression equation express a relationship between the regressand on the one hand and, on the other regressors that each represent different groups of closely related variables.

It is worth noting that the regression analysis gives only a few variables with significant correlations to variable A70 whereas the simple correlation analysis gave a large number

Summary

This regression analysis shows that, in this material, nasal airflow at a differential pressure of 10 mm H_2O after nose drops is influenced in the first place by size of adenoids. Other factors of importance in this respect appear to be the degree of prognathism and face width.

differential pressure of 10 mm H_2O before nose drops display only a moderate coefficient of determination $R^2 = 0.40$ It should be emphasized however that variable A67 has a large irregular error of method As will be seen from Table 5 (p 29) the error of method accounts for 30% of the variance for all the children in the study which means that one cannot expect R^2 to be higher than 0 70 The observed value should therefore be seen in relation to this maximum i.e (0 40/0 70) × 100 or just under 60% as an indication of the determinative value obtained with the regressors considered in this analysis

Size of adenoids as represented by the variable A20 proves to be the most important variable but by itself gives a relatively low coefficient of determination $R^2 = 0.20$ (see Table 26 p 73) It is conceivable that it occupies such a prominent position because the adenoidectomy children are overrepresented in relation to the controls

The skeletal variables A92 and A118 which represent sagittal depth of the bony nasopharynx, display the next strongest relationships with airflow before nose drops (A67) indicating that the greater the depth of the nasopharynx the greater the airflow

The variable for swollen nasal mucosa (A18) also displays a strong—negative—relationship with airflow before nose drops (A67)

The other regressors in the regression equation are only significant at the 5% level i e overjet (A55) height of corpus mandibulae (A44) and recurrent infections in the ear nose and throat (A06) As a regressor in the regression equation overjet (A55) is to be regarded as a consequence of mouth breathing and a low airflow rather than as a determinator of the airflow variable A67 Concerning the other two variables in the regression equation—A44 and A06—it is conceivable that their presence is a pure coincidence—in an analysis of sixty regression coefficients it is hardly surprising that two artefact coefficients reach the 5% level of significance This interpretation is supported by the non-significant simple correlation coefficients between A67 on the one hand and A44 and A06 on the other ($r = 0.0?$ and -0.18 respectively)

Summary

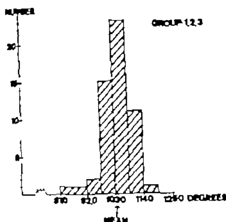
This regression analysis shows that the measurements of airflow in the present children at a differential pressure of 10 mm H_2O before nose drops (A67) are affected in the first place by size of adenoids, sagittal depth of the bony nasopharynx and the degree of swelling in the nasal mucosa Furthermore size of nasopharynx is shown to be of little importance for air flow in children with very large adenoids that impede the passage of air this also applies in children with no adenoids, since the passage of air is then sufficient regardless of the size of the nasopharynx It is only in the presence of small and moderate adenoids that size of nasopharynx is of essential importance for the magnitude of the nasal airflow

REGRESSAND· NASAL AIRFLOW PREOPERATIVELY AFTER NOSE DROPS

In the analysis presented in Table 37 the regressand was variable A70 Nasal airflow measured at a differential pressure of 10 mm H_2O after nose drops, and the regressors were the same as in the regression analysis with variable A67 as regressand The following regressors, given here in the order of introduction proved to be significant at the 1 % level. A20 A103 A80

Results and discussion

The regressors included in the regression equation as determinants of airflow at a differential pressure of 10 mm H_2O after nose drops (A70) have only a low coefficient of determination $R^2 = 0.32$. It should be noted however that these airflow measurements were difficult to reproduce exactly (the coefficient for the correlation between the initial value A70 and the value one month late A76 was 0 75 cf



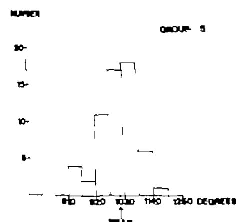


Fig 26. Distribution of children by size of the angle *IL/NSL*. The difference between the means for the adenoidectomy group and the controls is entirely ascribable to the low values in adenoidectomy group 5

be induced to follow the instructions. This analysis did not reveal any essential changes and does not call for any modification of the interpretations presented above

In a further multiple regression analysis with the interindividual difference between variables A70 and A67 as the regressand and the same regressors as before, none of the regressors in the equations tabulated above obtained significant corrrelation coefficients. This means that the regressors which are significant for variable A67 but not for A70 as regressand and vice versa can be substituted with correlated regressors (cf. variable A80 in the regression analysis with A70 as regressand) and that the regressors which proved significant in one of the analyses are on the verge of being significant in the other

EXPLANATORY VALUE OF DIFFERENT GROUPS OF REGRESSANDS THAT EXPRESS NASAL AIRFLOW

In the simple correlation analyses and multiple regression analyses, many regressors displayed significant relationships with the airflow regressands. In order to analyze the relative importance of different groups of regressors, these were divided into variables for age and sex, other anamnesis variables, adenoid, dentition and skeleton variables. These groups were then introduced into the analysis in different

Table 39 *Regressand. A46 Angle between upper incisors and nasion-sella line*

Regression coefficients, their std. error, level of significance (marked with asterisks), partial correlation coefficients, the total correlation coefficient (R^2), and the standard deviation of the residuals (R.S.D), in an analysis of 24 regressors

Regressor	Coefficient	Std. error	*t*-value	Partial corr
Constant	29.5600	17.4461	1.70	—
A49 M M upper	0.5894	0.2277	2.59	0.24
A56 Overbite	1.6145	0.4171	3.87	0.35
A79 Group	0.9955	0.3306	−3.01	−0.28
A90 sp–pn	0.4073	0.1094	3.72*	0.34
A96 Height of upper lip	0.6944	0.2874	2.41	0.23
A102 s–n–ss	0.5722	0.1585	3.61	0.33

R^2 0.39. R.S.D 5.48.

Table 38 *Determination coefficients (R^2) for groups of regressors in relation to the following regressands as expressions for nasal airflow A67 Preop airflow before nose drops A70 Preop airflow after nose drops A73 Postop airflow before nose drops A76 Postop airflow after nose drops*

Groups of regressors included in the analyses	Value of R^2 for regressands			
	A67	A70	A73	A76
Age + sex	0 02	0 04	0 00	0.03
Age + sex + skeleton variables	0 33	0.51	0.31	0.39
Age + sex + skeleton and adenoid variables	0.57	0.59	0.55	0.54
Age + sex + skeleton, adenoid and dentition variables	0.65	0.64	0 67	0 63
Age + sex + other anamnesis variables + adenoid, dentition and skeleton variables	0 70	0.66	0.72	0.64
Age + sex	0 02	0.04	0.00	0.03
Age + sex + adenoid variables	0 42	0.37	0.30	0.30
Age + sex + adenoid and dentition variables	0.53	0.43	0.47	0.47
Age + sex + adenoid dentition and skeleton variables	0 65	0.65	0 67	0.63
Age + sex + other anamnesis variables + adenoid, dentition and skeleton variables	0 70	0.66	0 72	0.64
Age + sex	0 02	0.04	0.00	0 03
Age + sex + dentition variables	0.20	0.27	0.29	0.30
Age + sex + dentition and skeleton variables	0.45	0.56	0.45	0.49
Age + sex + dentition adenoid and skeleton variables	0 65	0 64	0 67	0.63
Age + sex + other anamnesis variables + adenoid, dentition and skeleton variables	0.70	0 66	0.72	0.64

COMPARISON BETWEEN REGRESSANDS NASAL AIRFLOW BEFORE AND AFTER NOSE DROPS

A comparison between the regression analyses in which the regressands were nasal airflow at a differential pressure of 10 mm H_2O before (A67) and after (A70) nose drops respectively shows that size of adenoids as represented by variable A20 is the most important determinant for the magnitude of nasal airflow

The variable for swollen nasal mucosa (A18) only features in the analysis in which airflow before nose drops (A67) is the regressand A plausible explanation for this is that the nasal mucosa is decongested after nose drops (A70)

Skeletal variables that reflect the size of the nasopharynx are represented in both analyses, by variables A92 and A118 before nose drops (A67) and by variable A80 after nose drops (A70)

Concerning the other skeletal variables, degree of prognathism as represented by A103 features only in the analysis with variable A70 as the regressand

The dentition variables displayed weak correlations with airflow in both analyses.

The variables for year of birth and sex (A02 and A03) did not prove significant in either of these regression analysis.

In view of the fact that missing values for variables A67 and A70 amounted to approximately 15 % and chiefly referred to the adenoidectomy groups (groups 4 and 5 cf. Table 11 p 47) a separate regression analysis was made to determine whether the absence of the values has appreciably affected the conclusions drawn from the regression analyses in which these variables served as regressands In this regression analysis the missing airflow values were treated as 0 on the grounds that in most of the cases in which airflow could not be measured, the reason was total obstruction of the nasopharynx. The analysis does, however include a few cases that were expected to show normal airflow but where the child could not

The grouping variable (A79) is also in-
ided as a regressor in this regression equa
on. The negative relationship indicates that
etroclination of upper incisors was more com-
non among the children in the groups with a
igh number i.e. the adenoidectomy groups
4 and 5).

The variable for upper arch width between
irst molars (A49) is also included in the regres-
ion equation as a determinant of variable A46
n this case the relationship is positive.

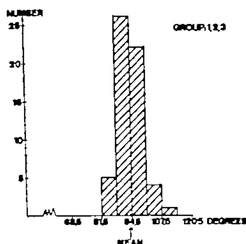
Length of upper lip (A96) shows a negative
lmost significant relationship in the regression
quation with the angle between the upper in-
isors and the nasion-sella line.

Thus, retroclination of upper incisors in rela-
ion to the nasion-sella line appears to be
requent in children with a small lower face
eight, large overbite, long upper lip a small
alue for the angle s–n–ss and a narrow upper
rch between first molars such retroclination
was also more common among the present
adenoidectomy children than among the con-
trols.

Discussion

Of the regressors that are included in the regression equation, the variables A56, Overbite, A90, Anterior lower face height, and A102, Angle between sella turcica—nasion—subspinale, are highly significant ($P < 0.001$) The group variable A79 is significant at the 1% level. The other regressors—A49 Upper arch width between first molars, and A96 Height of upper lip—are significant at the 5% level. The relationships between the regressand and the various regressors must be considered to have an underlying cause in common.

It is conceivable, however that there is a causal relationship in the negative correlation between the regressand and regressor A96 retroclination of the upper incisors being regarded as a consequence of increased lip pressure from a long upper lip and altered muscle balance when the mouth is held open in mouth breathing.



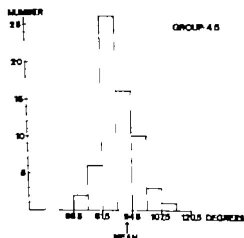


Fig 28 Distribution of children by size of the angle *IL/ML*. The difference between the means for the adenoidectomy group and the controls is entirely ascribable to the low values in adenoidectomy group 5.

The determinative value of the grouping variable (A79) is probably a reflection of determination from variables for mode of breathing, adenoids and airflow It is therefore particularly interesting that regressor A79 indicates that retroclination of the upper incisors is more frequent among the adenoidectomy children than among the controls.

The circumstance that about 81% of the adenoidectomy children—all of whom had large adenoids—were mouth breathers suggests that mouth breathers have more retro-

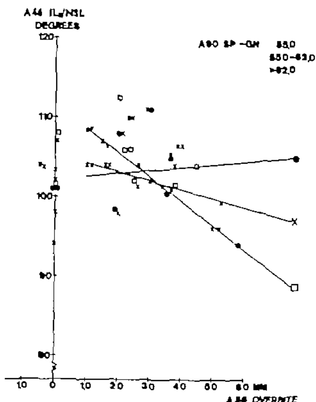


Fig 27 Relationship between the regressand A46 and the regressors A56 size of vertical overbite and A90 lower face height The values of each hild are marked by a plot Separate regression lines for different values for lower face height have been obtained with the computer The diagram indicates that the relationship between the regressand A46 and the regressor A56 is appreciable only for low values of A90 lower face height It is worth noting that the children with high values for lower face height include the largest number of mouthbreathers.

sequences—though always with age and sex first and other anamnesis variables last—in order to study the resultant increment to the coefficient of determination (see Table 38)

Table 38 shows that the explanatory value of age and sex is slight and that the adenoid variables and the skeleton variables each have a higher coefficient of determination than the dentition variables with respect to the regressands A67 and A70 In the case of regressands A73 and A76 the skeleton variables have the highest explanatory value while the adenoid and dentition variables have the same coefficient.

The anamnesis variables appear to be important for regressands A67 and A73 i.e only before nose drops

Taken together the variables for age and sex and the adenoid, dentition and skeleton variables display approximately the same explanatory value for each of the airflow variables

REGRESSAND ANGLE BETWEEN UPPER INCISORS AND NASION SELLA LINE

In the analysis presented in Table 39 the regressand was variable A46 Angle between upper incisors and nasion-sella line and the regressors were as follows anamnesis variables A02–03 A15–16 adenoid variable A20 dentition variables A49 A55–56 A60–61 group variable A79 airflow variables A67 A70 skeleton variables A88 A90–92 A96–97 A101–102 A106–108 The regressors included in the regression equation were introduced in the following order A102, A79 A56 A90 A49 and A96

The distribution of the control and adenoidectomy children with respect to the regressand is shown in Fig. 26

Results

The regressors included in the regression equation as determinants of the regressand A46 have a *moderate coefficient of determination* $R^2 = 0\ 39$ *If one also includes all the regressors enumerated above that are not significant* at the 5% level the coefficient of determination increases to 0 45

The variables that are highly significant or significant ($P < 0\ 001$ $P < 0\ 01$ respectively) have the expected sign

The strongest relationships with this regressand concern the variables that express lower face height (A90) and overbite (A56) These relationships indicate that retroclination of upper incisors in relation to the nasion-sella line is frequently found in children with a small lower face height and large overbite (cf Fig 27)

The variable for the angle s–n–ss (A102) displays the next strongest relationship with the measure of retroclination (A46)

e grouping variable (A79) is also in- d as a regressor in this regression equa- The negative relationship indicates that clination of upper incisors was more com- among the children in the groups with a number i.e. the adenoidectomy groups d 5).

e variable for upper arch width between molars (A49) is also included in the regres- equation as a determinant of variable A46 is case the relationship is positive.

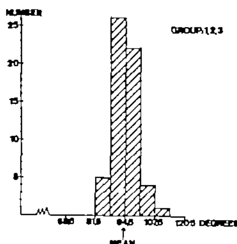
ngth of upper lip (A96) shows a negative t significant relationship in the regression tion with the angle between the upper in- s and the nasion-sella line.

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ussion

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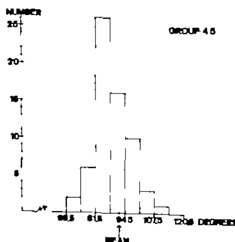


Fig 28 Distribution of children by size of the *angle IL/ML*. The difference between the means for the adenoidectomy group and the controls is entirely ascribable to the low values in adenoidectomy group 5

The determinative value of the grouping variable (A79) is probably a reflection of determination from variables for mode of breathing, adenoids and airflow It is therefore particularly interesting that regressor A79 indicates that retroclination of the upper incisors is more frequent among the adenoidectomy children than among the controls.

The circumstance that about 81% of the adenoidectomy children—all of whom had large adenoids—were mouth breathers suggests that mouth breathers have more retro-

Table 40 *Regressand A48 Angle between lower incisors and mandibular line*

Regression coefficients, their std. error level of significance (marked with asterisks), partial correlation coefficients, the total correlation coefficient (R^2), and the standard deviation of the residuals (R.S.D), in an analysis of 23 regressors

Regressor	Coefficient	Std. error	t-value	Partial corr
Constant	113 1500	2.6688	42.40	—
A15 Mouth breathing	−5.0374	0.9946	−5.06	−0.42
A55 Overjet	1 3701	0.3286	4 17	0.36
A107 ML/NL	−0 6548	0.0949	−6.90	−0.54

$R^2 = 0\ 48$ R.S D = 5 14

clined incisors Similar results have been reported by Leech (1958) in a study which showed that Angle Cl II 2 is more frequent than Cl II 1 in individuals with large adenoids Thus the present results do not support the frequently expressed opinion that mouth breathers usually have proclined upper incisors e g Angle (1907) Strang (1933) Bowen & Balyeat (1934) McCoy (1941) Johnson (1942) Ballenger & Ballenger (1943) Massler Poncher & Schour (1945) Giacometti (1947) Subtelny (1954) Negus (1955) Duyzing (1963) and Moyers (1963)

Summary

This multiple regression analysis shows that retroclined upper incisors are frequently found in children with a small lower face height, large overbite long upper lip small value for the angle s–n–ss and a narrow upper arch and that such retroclination was more common among the present adenoidectomy children than among the controls The relationships between the regressand and the various regressors may be regarded as having an underlying cause in common There may also be a causal negative almost significant relationship between inclination of upper incisors and length of upper lip a conceivable explanation being that retroclination of the upper incisors is a consequence of increased lip pressure from a long upper lip and an altered muscle balance when the mouth is held open in mouth breathing

REGRESSAND ANGLE BETWEEN *LOWER INCISORS AND MANDIBULAR LINE*

In the analysis presented in Table 40 the regressand was variable A48 Angle between lower incisors and mandibular line, and the regressors were as follows anamnesis variable A02–03 A15–16 adenoid variable A20 dentition variables A49 A55–56 A60 group variable A79 airflow variables A67 A70 skeleton variables A88 A90–92, A96–97 A101 A103 A106–108 The regressors were introduced in the following order A107 A15 A55

The distribution of the control and adenoidectomy children with respect to the regressand is shown in Fig 28

Results

The regressors included in the regression equation as determinants of the regressand (A48) display a moderate coefficient of determination, $R^2 = 0\ 48$ If one also includes all the regressors enumerated above that are not significant at the 5% level the coefficient is increased to 0.58 The variables that are highly significant ($P < 0\ 001$) display the expected sign

Variable A107 Angle between mandibular and nasal lines, displays the strongest relationship with the regressand in this analysis By itself this variable has a coefficient of determination $R^2 = 0\ 28$ (see Table 23 p 67) The relationship indicates that children with a large

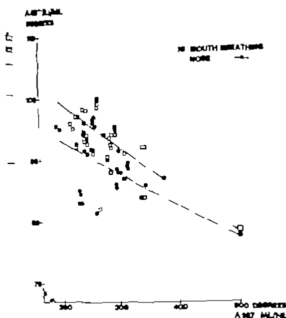


Fig. 29. Diagram showing the relationship between the regressand A48 and the regressor A107 angle between the mandibular and nasal lines, nosebreathers and mouthbreathers being denoted with different symbols. The sizes of each child are marked by plot. Separate regression lines for the two modes of breathing have been obtained with the computer. The diagram indicates that the regression line for nosebreathers lies higher than for mouthbreathers and that variable A48 decreases with increasing values of variable A107.

angle between the mandibular and nasal lines commonly display retroclination of the lower incisors.

The next strongest relationship with the regressand concerns variable A15 Mouth breathing. Thus, the mouth breathers in this study more frequently had retroclined lower incisors (cf. Fig. 29).

Variable A55 Overjet, is also included as a regressor in this regression equation. The relationship indicates that the children with a large overjet frequently had proclined lower incisors.

The regression analysis thus shows that retroclination of the lower incisors in relation to the mandibular line is common among children with a large angle between the mandibular and nasal lines, small overjet and mouth breathing.

Discussion

All the regressors included in the regression equation are highly significant ($P < 0.001$).

The strong relationship between inclination of the lower incisors and the angle between the mandibular and nasal lines should be seen in the first place as a parallel to the circumstance that this inclination was measured in relation to the mandibular line.

The relationship between retroclination of the lower incisors and mouth breathing can further be interpreted as a consequence of the lip muscles acting on the lower incisors when the mouth is held open in mouth breathing. This may possibly lead to increased tension in the orbicularis oris muscle, resulting in posterior pressure against the incisors because the tendon plates attaching this muscle at the angles of the mouth are held back in turn by the buccinator, zygomaticus major and caninus muscles (Petrén 1948).

A *low tongue position in mouth breathing* (see Table 19, cf. Subtelny 1954, Holik, 1957, Ricketts, 1958 a), with the tongue possibly held withdrawn as well, may also have contributed to retroclination of the lower incisors due to reduced tongue pressure against the lingual surface of these teeth.

The positive relationship between overjet (A55) and the regressand (A48) reflects the circumstance that these two variables have the same underlying mechanism.

Summary

This multiple regression analysis shows that retroclination of the lower incisors is common among children who have a large angle between the mandibular and nasal lines, a small overjet and mouth breathing.

The retroclination of lower incisors in the present children is considered in part to be a consequence of posterior rotation of the lower jaw under the influence of the lip muscles and/or reduced tongue pressure against the lingual surface of the lower incisors when the tongue is held low in mouth breathing, and in part to reflect constitutional factors.

Table 40 *Regressand A48 Angle between lower incisors and mandibular line*

Regression coefficients, their std. error level of significance (marked with asterisks), partial correlation coefficients, the total correlation coefficient (R^2), and the standard deviation of the residuals (R.S.D), in an analysis of 23 regressors

Regressor	Coefficient	Std. error	t value	Partial corr
Constant	113 1500	2.6688	42.40	—
A15 Mouth breathing	−5 0374	0.9946	−5 06	−0.42
A55 Overjet	1.3701	0.3286	4 17	0.36
A107 ML/NL	−0.6548	0 0949	−6.90	−0.54

$R^2 = 0.48$ R.S.D = 5 14

clined incisors Similar results have been reported by Leech (1958) in a study which showed that Angle Cl II 2 is more frequent than Cl II 1 in individuals with large adenoids Thus the present results do not support the frequently expressed opinion that mouth breathers usually have proclined upper incisors e g. Angle (1907) Strang (1933) Bowen & Balyeat (1934) McCoy (1941) Johnson (1942) Ballenger & Ballenger (1943) Massler Poncher & Schour (1945) Giacometti (1947) Subtelny (1954) Negus (1955) Duyzing (1963) and Moyers (1963)

Summary

This multiple regression analysis shows that retroclined upper incisors are frequently found in children with a small lower face height, large overbite, long upper lip small value for the angle s–n–ss and a narrow upper arch and that such retroclination was more common among the present adenoidectomy children than among the controls. The relationships between the regressand and the various regressors may be regarded as having an underlying cause in common There may also be a causal negative almost significant relationship between inclination of upper incisors and length of upper lip a conceivable explanation being that retroclination of the upper incisors is a consequence of increased lip pressure from a long upper lip and an altered muscle balance when the mouth is held open in mouth breathing

REGRESSAND ANGLE BETWEEN LOWER INCISORS AND MANDIBULAR LINE

In the analysis presented in Table 40 the regressand was variable A48 Angle between lower incisors and mandibular line, and the regressors were as follows anamnesis variables A02–03 A15–16 adenoid variable A20 dentition variables A49 A55–56 A60 group variable A79 airflow variables A67 A70 skeleton variables A88 A90–92 A96–97 A101 A103 A106–108 The regressors were introduced in the following order A107 A15 A55

The distribution of the control and adenoidectomy children with respect to the regressand is shown in Fig. 28

Results

The regressors included in the regression equation as determinants of the regressand (A48) display a moderate coefficient of determination. $R^2 = 0.48$ If one also includes all the regressors enumerated above that are not significant at the 5% level the coefficient is increased to 0 58 The variables that are highly significant ($P < 0.001$) display the expected sign

Variable A107 Angle between mandibular and nasal lines displays the strongest relationship with the regressand in this analysis By itself this variable has a coefficient of determination $R^2 = 0.28$ (see Table 23 p 67) The relationship indicates that children with a large

Table 41 *Regressand. A49 Upper arch width between first molars*

Regression coefficients, their std. error, level of significance (marked with asterisks), partial correlation coefficients, the total correlation coefficient (R^2), and the standard deviation of the residuals (R.S.D.), in an analysis of 40 regressors

Regressor	Coefficient	Std. error	t-value	Partial corr
Constant	27.7980	4.2970	6.47	—
A53 Length of upper arch	0.1962	0.0724	2.74	0.24
A57 Sagittal rel. M_1–M_1 right	0.1987	0.0625	3.18	0.28
A64 Space difference upper	0.1310	0.0324	4.04	0.35
A101 Vol. of nasopharynx	0.6166	0.1097	5.62*	0.46
A107 ML/NL	−0.0935	0.0332	−2.82	−0.25
A113 lo–lo/n–gn	0.0697	0.0336	2.07	0.19

R^2 0.51 R.S.D. 1.72

As will be seen from Table 42, the coefficient of determination is reduced to $R^2 = 0.35$

In this regression equation, the regressors are the same skeleton variables as before plus A82, Nose width over alae nasii.

According to both these regression analyses, the size of the variable for upper arch width between first molars (A49) appears to be determined chiefly by the skeleton and dentition variables (cf. Fig. 31)

Thus, a narrow upper arch between the first molars appears to be common among children with a small nasopharynx, a long, narrow face, a short, crowded upper jaw and a large angle between the upper and lower jaws, i.e. between the nasal and mandibular lines.

Discussion

The regressors that are significant at the 1% and 0.1% levels in the regression equation are dominated by variables representing the size of the upper jaw The value of these variables as determinants of upper arch width between the first molars is to be regarded as a parallel phenomenon between regressand and regressors rather than as a causal relationship

Concerning the skeleton variables denoting the volume of the bony nasopharynx and an index for face width/face height, it is again difficult to see a causal relationship between these and the variable for upper arch width between the first molars. These relationships should also be interpreted as parallel phenomena in the sense that a narrow upper jaw is common among children with a narrow type of face and little space in the nasopharynx. A significant positive relationship between face width and arch width has been demonstrated previously by Lundström & Lysell (1953) Linder Aronson & Bäckström (1960) Linder Aronson (1963), Solow (1966) and Slagsvold (1969)

The significant relationships demonstrated in the simple correlation analyses for upper arch width between first molars on the one hand and, on the other the angles between the mandibular line and the nasal (A107) and nasion-

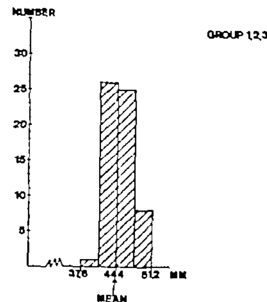
Table 42. *Regressand. A49 Upper arch width between first molars*

Same regressors as in Table 41 apart from the dentition variables

Regressor	Coefficient	Std. error	t-value	Partial corr
Constant	27.4020	5.1012	5.37	—
A82 Nose width over alae nasii	0.2300	0.0912	2.52	0.22
A101 Vol. of nasopharynx	0.6522	0.1223	5.33 **	0.43
A107 ML/NL	0.0971	0.0370	−2.63	−0.[illegible]3
A113 lo–lo/n–gn	0.0773	0.0385	2.02	0.18

R^2 0.35 R.S.D. 1.97

7 [illegible]



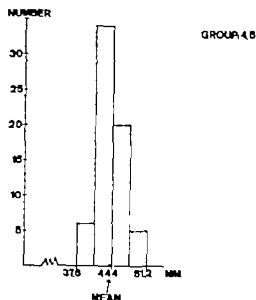


Fig 30 Distribution of children by *width of upper arch between the first molars* The distribution is the same for the adenoidectomy group and the controls.

REGRESSAND· UPPER ARCH WIDTH BETWEEN FIRST MOLARS

In the analysis presented in Table 41 the regressand was variable A49 Upper arch width between first molars, and the regressors were as follows anamnesis variables A02–03 A13–14 adenoid variables A20 A32 A38 A40 dentition variables A46–48 A53–54 A56–57 A61 group variable A79 airflow variables A67 A70 A73 A76 skeleton variables A80 A82, A85–87 A91–92 A94 A100–103 A105–107 A113 A121 A123 and A126. The regressors were introduced in the following order A61 A101 A107 A57 A53 and A113

The distribution of the control and adenoidectomy children with respect to the regressand is shown in Fig. 30

Results

The regressors included in the regression equation as determinants of upper arch width give a coefficient of determination $R^2 = 0.51$

Volume of bony nasopharynx (A101) is the variable in this regression analysis that has the stronecst relationship with width of upper arch between first molars By itself however this *variable has a coefficient of determination* of no more than 0 17 (see Table 23 p 67)

Variable A61 Space difference of upper arch, displays the next strongest relationship with width of upper arch.

The variable for the sagittal relationship between the mesial surfaces of the upper and lower first molars on the right side (A57) also *appears to be related to the width of the upper* arch between the first molars.

Furthermore the regression analysis shows that children with a narrow upper arch between the first molars have a large angle between *the mandibular and nasal lines* (A107)

The relationship between length (A53) and width (A49) of upper arch (see Table 20, p 63) is also demonstrated in this regression analysis which shows that the former variable is a *determinant of the latter*

Another finding is that the index for face width face height (A113) appears to be of some importance in determining the width of the upper arch between the first molars

In order to study *to what extent the dentition* variables included as regressors contributed to the determination of regressand A49 a second analysis was made with the same regressand and the same regressors apart from the *dentition* variables.

Table 41 *Regressand. A49 Upper arch width between first molars*

Regression coefficients, their std. error level of significance (marked with asterisks), partial correlation coefficients, the total correlation coefficient (R^2), and the standard deviation of the residuals (R.S.D.), in an analysis of 40 regressors

Regressor	Coefficient	Std. error	*t*-value	Partial corr
Constant	27 7980	4.2970	6 47	—
A53 Length of upper arch	0.1982	0 0724	2.74	0.24
A57 Sagittal rel. M_1–M right	0.1987	0 0625	3.18	0.28
A61 Space difference upper	0.1310	0.0324	4.04	0.35
A101 Vol of nasopharynx	0.6166	0.1097	5.62	0.46
A107 ML/NL	0.0935	0.0332	2.82	−0.25
A113 lo–lo'n–gn	0.0697	0.0336	2 07	0.19

R^2 0.51 R.S.D. 1 72

As will be seen from Table 42, the coefficient of determination is reduced to $R^2 = 0.35$

In this regression equation, the regressors are the same skeleton variables as before plus A82, Nose width over alae nasii.

According to both these regression analyses, the size of the variable for upper arch width between first molars (A49) appears to be determined chiefly by the skeleton and dentition variables (cf Fig. 31)

Thus, a narrow upper arch between the first molars appears to be common among children with a small nasopharynx, a long, narrow face, a short, crowded upper jaw and a large angle between the upper and lower jaws, i.e. between the nasal and mandibular lines.

Discussion

The regressors that are significant at the 1% and 0.1% levels in the regression equation are dominated by variables representing the size of the upper jaw The value of these variables as determinants of upper arch width between the first molars is to be regarded as a parallel phenomenon between regressand and regressors rather than as a causal relationship

Concerning the skeleton variables denoting the volume of the bony nasopharynx and an index for face width/face height, it is again difficult to see a causal relationship *between* these and the variable for upper arch width between the first molars. These *relationships* should also be interpreted as parallel phenomena in the sense that *a narrow upper jaw is* common among children with a narrow type of face and little *space in the nasopharynx*. A significant positive relationship between face *width and arch width* has been demonstrated previously by Lundström & Lysell (1953), Linder Aronson & Bäckström (1960), Linder Aronson (1963) Solow (1966) and Slagsvold (1969)

The significant relationships demonstrated in the simple correlation analyses for upper arch width between first molars on the one hand and, on the other the angles between the mandibular line and the nasal (A107) and nasion-

Table 42. *Regressand A49 Upper arch width between first molars*

Same regressors as in Table 41 apart from the dentition variables

Regressor	Coefficient	Std. error	*t*-value	Partial corr
Constant	27 4020	3.1012	5.37	—
A82 Nose width over alae nasi	0.2300	0.0912	2.52	0.22
A101 Vol. of nasopharynx	0.6522	0.1223	5.33	0.43
A107 ML/NL	−0.0971	0.0370	−2 63	−0.23
A113 lo–lo'n–gn	0.0773	0 0383	2.07	0.18

R^2 0.35 R.S.D. 1.97

7 00037

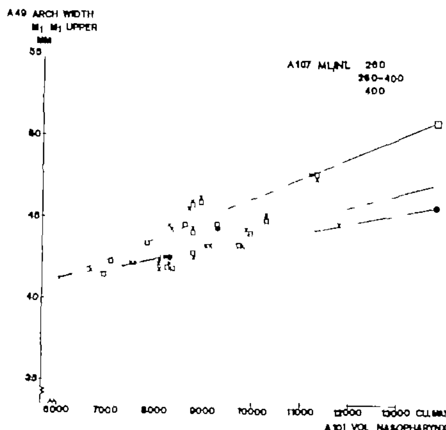


Fig 31 Diagram showing the relationship between the regressand A49 and the regressors A101 volume of nasopharynx and A107 the angle ML/NL. Separate regression lines for different values of the angle ML/NL have been obtained with the computer The diagram indicates that the relationship between the regressand A49 and the regressor A101 is appreciable only for low values of the angle ML/NL. It is worth noting that the children with high values for the angle ML/NL include the largest number of mouthbreathers.

sella lines (A106)—cf Table 23 p 67—are represented in the regression equation by variable A107 The relationship indicates that children with a narrow upper arch more frequently display large angles between the mandibular line and the nasal and nasion-sella lines

These relationships are supported by the highly significant correlation ($r = 0\ 26$ P 0 001) in the simple correlation analysis (cf Table 20 p 63) between variable A49 and variable A56 Overbite since the latter variable has been shown to be related with the variables representing the angles between the mandibular line and the nasal and nasion-sella lines (A107 and A106 respectively cf Table 23 p 67)

It is particularly noteworthy that the significant correlations obtained in the simple correlation analysis between A49 and the airflow variables A70 A73 and A76 (cf Table 22 p 65) have not appeared in the present regression equation as determinants of upper arch width between first molars. Since highly significant correlations have been found between the variables for airflow after nose drops (A70 and A76) and variable A101 Volume of bony nasopharynx ($r = 0\ 32$ and 0 37 respectively $P < 0\ 001$ cf Table 30 p 77) and since the latter variable is one of the regressors in the present regression equation it has probably served to reflect the relationship between A49 and the airflow variables

The determinants in the regression equation do not include any of the adenoid variables either i.e A20 A32, A38 and A40 According to the regression analyses for mouth breathing (A15 p 84) and airflow (A67 p 87) these two factors are influenced in the first place by size of adenoids and size of nasopharynx Since the variables for size of adenoids have

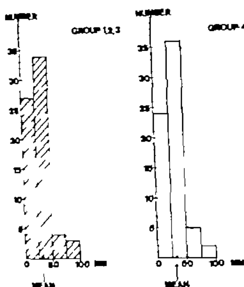


Fig 32. Distribution of children by size of *overjet* The distribution appears asymmetric in the adenoidectomy group as well as in the control group—neither group has many children with overjet 5 mm.

been assessed and measured in relation to the size of nasopharynx, the regressor A101 probably also reflects the significant relationships demonstrated in the simple correlation analyses between the adenoid variables and upper arch width between first molars (= −0.27 and −0.30 respectively $P<0.001$ cf. Table 21 p 64)

Summary

The multiple regression analyses show that the width of the upper arch between the first molars is largely determined in these children by the skeleton and dentition variables. A narrow upper arch is common among children with a small nasopharynx, a long, narrow face, a narrow nose, a short, crowded upper jaw and a large angle between the nasal and mandibular lines.

According to this analysis, a narrow upper arch between the first molars in these children is in the first place a parallel phenomenon to their long, narrow type of face with a small nasopharynx and narrow nose. This, however does not rule out the possibility of a causal relationship between upper arch width and adenoids, with mouth breathing and a low tongue position as a result. This can be investigated best by follow-up studies after adenoidectomy

REGRESSAND OVERJET

In the analysis presented in Table 43 the regressand was variable A55 Overjet, and the regressors were as follows. anamnesis variables *A02–03 A15* adenoid variable A20 dentition variables A53 A57–58 A65 airflow variables A67 A70 group variable A79 skeleton variables A85–87 A91 A96, A105 A126–127 tongue position variable A129 The regressors were introduced in the following order A105 A126 A57 A53 and A15

The distribution of the control and adenoidectomy children with respect to the regressand is shown in Fig. 32.

Table 43 *Regressand A55 Overjet*

Regression coefficients, their std. error level of significance (marked with asterisks), partial correlation coefficients, the total correlation coefficient (R^2), and the standard deviation of the residuals (R.S.D), in an analysis of 20 regressors

Regressor	Coefficient	Std. error	*t*-value	Partial corr
Constant	13 1630	2,7231	4.83	—
A15 Mouth breathing	0 5083	0.2186	2.32*	0.20
A53 Length of upper arch	0.2190	0.0528	4.15	0.34
A57 Sagittal rel. M_1–M_1 right	0.2354	0 0556	4.23	0.35
A105 n–n–ar	0.2940	0.0488	6.02	0.47
A126 n–ho	0 0980	0.0334	2.94	0.25

R^2 0 46 R S D 1.22

* [illegible]

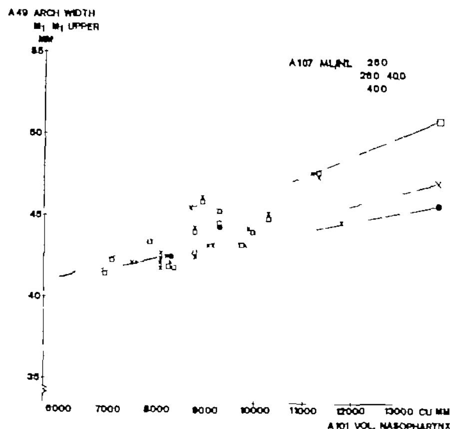


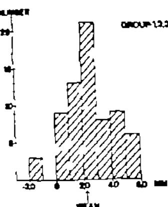
Fig 31 Diagram showing the relationship between the regressand A49 and the regressors A101 olume of nasopharynx and *A107* the angle ML/NL. Separate regression lines for different values of the angle ML/NL have been obtained with the computer The diagram indicates that the relationship between the regressand A49 and the regressor A101 is appreciable only for low values of the angle ML/NL. It is worth noting that the children with high values for the angle ML/NL include the largest number of mouthbreathers.

sella lines (A106)—cf Table 23 p 67—are represented in the regression equation by variable A107 The relationship indicates that *children with a narrow upper arch more frequently display large angles between the mandibular line and the nasal and nasion sella lines*

These relationships are supported by the highly significant correlation ($r = 0.26$ P 0.001) in the simple correlation analysis (cf Table 20 p 63) between variable A49 and variable A56 Overbite, since the latter variable has been shown to be related with the variables representing the angles between the mandibular line and the nasal and nasion-sella lines (A107 and A106 respectively cf. Table 23 p 67)

It is particularly noteworthy that the significant correlations *obtained in the simple correlation* analysis between A49 and the airflow variables A70 A73 and A76 (cf Table 22 p 65) have not appeared in the present regression equation as determinants of upper arch width between first molars. Since highly significant *correlations have been found between* the variables for airflow after nose drops (A70 and A76) and variable A101 Volume of bony *nasopharynx* ($r = 0.32$ *and* 0.37 *respectively* $P < 0.001$ cf Table 30 p 77) and since the latter variable is one of the regressors in the present regression equation it has probably served to reflect the relationship between A49 and the airflow variables.

The determinants in the regression equation do not include any of the adenoid variables either i.e. A20 A32 A38 and A40 According to the regression analyses for mouth breathing (A15 p 84) and airflow (A67 p 87) these two factors are influenced in the first place by size of adenoids and size of nasopharynx. Since the variables for size of adenoids have



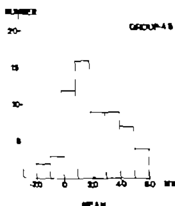


Fig 33 Distribution of children by size of overbite. The distribution is the same for the adenoidectomy group and the controls.

a postnormal occlusion with proclined upper incisors, an opinion expressed by Angle (1907) in his description of Cl. II division 1 malocclusions

Summary

This multiple regression analysis shows that large overjet is common among children with a large value for the angle ss–n–sm, a long upper arch, large sagittal length of the roof of the nasal cavity and a postnormal relation between the upper and lower first molars, and mouth breathing.

The size of overjet in the present children appears to be largely a parallel phenomenon to the sagittal relationship between the upper and lower jaws as well as to the sagittal length of the roof of the nasal cavity and of the upper arch.

REGRESSAND: OVERBITE

In the analysis presented in Table 44 the regressand was variable A56, Overbite and the regressors were as follows. anamnesis variables A02–03 A10 dentition variables A49 A60 A63 airflow variables A67 A70 skeleton variables A80 A85–87 A89 A91 A94 A101 A106–107 A116 A121 A126–127 The regressors were introduced in the following order A63 A02, A116 and A127

The distribution of the control and adenoidectomy children with respect to the regressand is shown in Fig. 33

Results

The regressors included in the regression equation as determinants of the size of overbite display a moderate coefficient of determination.

Table 44 *Regressand A56 Overbite*

Regression coefficients, their std. error level of significance (marked with asterisks), partial correlation coefficients, the total correlation coefficient (R^2), and the standard deviation of the residuals (R.S.D), in an analysis of 22 regressors

Regressor	Coefficient	Std. error	*t*-value	Partial corr
Constant	10.6240	6.2146	1.71	—
A02 Year of birth	0.1576	0.0614	2.56	0.22
A63 M M lower M_1–M upper	0.1154	0.0256	4.51	0.37
A116 n–sp –gn	0.1982	0.0593	3.34	0.29
A127 s–ho	0.1470	0.0577	2.54	0.22

R^2 0.33 R.S.D 1.16.

Results

The regressors included in the regression equation as determinants of the size of overjet have a moderate coefficient of determination $R^2 = 0\ 46$ If one also includes all the regressors enumerated above that are not significant at the 5% level, the coefficient of determination is increased only to 0 52. The variables that are significant at the 1% and 0 1% levels display the expected sign

In this regression analysis the strongest relationship with size of overjet is displayed by variable A105 Angle subspinale-nasion-supramentale By itself this variable has a coefficient of determination $R^2 = 0.25$ (cf Table 23 p 66) The next strongest relationship with overjet is displayed by variable A57 Sagittal relation between the mesial surfaces of upper and lower first molars on the right side

Variable A53 Length of upper arch, also appears to be important for determining the size of overjet as does variable A126, which expresses the sagittal length of the roof of the nasal cavity

The regression analysis also indicates that variable A15 Mouth breathing, is of some importance for size of overjet but this relationship is significant only at the 5% level

Large overjet thus appears to be common among children with large values for the angle subspinale nasion-supramentale a long upper arch, large sagittal length of the roof of the nasal cavity a postnormal relationship between the upper and lower first molars and mouth breathing.

Discussion

The variables that are significant at the 1% or 0 1% level in the regression equation represent jaw relationships in the sagittal plane (A105 A57) a sagittal dimension on the roof of the nasal cavity (A126) and length of upper arch (A53)

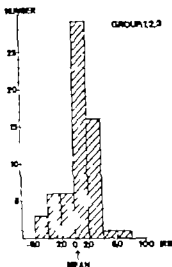
The relationships between regressand A55 Overjet, and these four regressors are to be regarded as parallel phenomena in that the size of overjet is influenced by sagittal displacement in the relationship between upper and lower jaw (A105 A57) or the size of the sagittal depth of the upper jaw (A126 A53)

A possible explanation for the almost significant relationship ($P < 0\ 05$) between variable A15 Mouth breathing, and large overjet is that the sagittal relationship between the upper and lower jaws increases in connection with posterior rotation of the lower jaw in mouth breathing

The frequently expressed opinion that individuals who breath through the mouth have a large overjet as a consequence of proclined upper incisors (Angle, 1907 Strang 1933 McCoy 1941 Ballenger & Ballenger 1943 Giacometti 1947 Negus 1955 Duyzing 1963) is not supported by this regression analysis since the variables that express the inclination of the upper and lower incisors (A46 and A48 respectively) have not featured as regressors. Instead, the results indicate that the children who were mouth breathers and who underwent adenoidectomy had more retroclined upper and lower incisors than the controls. The differences between the adenoidectomy and control groups in this respect are 6 6 and 7.3 respectively and are significant at the 0 1% level (cf Table 9 p 41)

The regression analyses in which the regressands are the variables for the inclination of the upper and lower incisors (A46 and A48 respectively) also indicate that the adenoidectomy children had a greater degree of retroclination

If the variable for overjet is regarded as an expression for the sagittal relationship between the upper and lower jaws frontally as well as laterally and if the size of overjet increases in mouth breathing the results obtained appear to support the opinion put forward by James & Hastings (1932) namely that mouth breathing accentuates the postnormal relationship in persons with a natural postnormal tendency It has not been found, on the other hand, that mouth breathers usually have



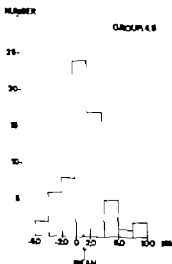


Fig. 34 Distribution of children in accordance with the *sagittal relationship between the mesial surfaces of the right first molars in the upper and lower jaws.* The distribution is the same in the adenoidectomy group and the controls

15 p 56), which showed a highly significant correlation ($r = -0.40$, $P < 0.001$) for the relationship between overbite and year of birth. These results fully agree with earlier reports by Seipel (1946), Baume (1950) and Moorees (1959). The increase in overbite with increasing age can be explained in terms of the difference in crown height between the deciduous and permanent incisors. Overbite involving the incisors thus increases in absolute terms from the deciduous to the permanent dentition but is not changed in relative terms (Moorees 1959) Approximately 35% of the children in this study had deciduous incisors

No significant relationships were found for the airflow regressors in this regression analysis

Summary

This multiple regression analysis shows that a small overbite is common among children with crossbite or a tendency to crossbite, a small value for the relationship between anterior upper and total face height, and a small posterior upper face height. A small overbite was also found more frequently among the younger children.

The size of overbite in the children in this study is considered to be a parallel phenomenon to crossbite or a tendency to crossbite and to the size of upper face height.

The increase in overbite with increasing age is considered to be a consequence of the difference in crown height between the deciduous and permanent incisors.

REGRESSAND SAGITTAL RELATIONSHIP BETWEEN MESIAL SURFACES OF UPPER AND LOWER RIGHT FIRST MOLARS

In the analysis presented in Table 45 the regressand was variable A57 Sagittal relationship between mesial surfaces of upper and lower right first molars, and the regressors were as follows. anamnesis variables A02–03 dentition variables A48 A55 airflow variables A67 A70 group variable A79 skeleton variables A85 A105 A113 tongue-position variable A1 9 The regressors were introduced in the following order A55 A113 A85 A105 and A03

The distribution of the control and adenoidectomy children with respect to the regressand is shown in Fig. 34

$R^2 = 0.33$ If one also includes all the regressors enumerated above that are not significant at the 5% level the coefficient increases only to 0.41 The variables that are significant at the 1% and 0.1% levels display the expected sign

The regressor that displays the strongest relationship with overbite is variable A63 which expresses the relationship between the widths of the lower and upper arches between the first molars The coefficient of determination for this variable alone is $R^2 = 0.23$ (cf Table 20 p 63)

The next strongest relationship with overbite is displayed by variable A116 which expresses the relationship between anterior upper face height (A89) and total face height (A88) In the simple correlation analysis, anterior upper face height (A89) showed a significant correlation ($r = 0.34$) with overbite (A56) but total face height (A88) did not (cf Table 23 p 66) The relationship obtained for the index variable in the regression analysis is therefore to be regarded in the first place as a reflection of the relationship between anterior upper face height and overbite

The regression analysis also shows that year of birth (A02) is involved in determining the size of overbite The negative almost significant relationship indicates that the children in this study with a low year of birth i e relatively high age, have a larger overbite than the younger children.

Variable A127 which represents the approximate vertical dimension of the body of the sphenoid bone, is also shown by the regression analysis to be related to size of overbite The simple correlation analysis indicated that this variable is closely related ($r = 0.67$) with variable A94 Posterior upper face height (cf Table 31 p 78) The almost significant relationship indicated in the regression analysis between variable A127 and overbite can therefore also be regarded as a reflection of the relationship between posterior upper face height and overbite

A small overbite is thus common in this study among children with a large value for the relationship between the widths of the lower and upper arches, i e. crossbite or a tendency to crossbite, a small value for the relationship between anterior upper and total face height a small posterior upper face height and a high year of birth i e low age.

Discussion

Of the regressors that are included in the regression equation the variable A63 Crossbite, is highly significant ($P < 0.001$) The variable A116 Index for the relationship between upper anterior and total face height is significant at the 1% level The other regressors—A02, Year of birth, and A127 Approximate vertical dimension of the body of the sphenoid bone—are significant at the 5% level.

According to this regression analysis, the size of overbite is largely determined by variable A63 i e crossbite or a tendency to crossbite.

The relationship between crossbite and small overbite can be interpreted as a parallel phenomenon If the lower jaw displays an anterior position in relation to the upper jaw there will be a greater probability of crossbite as well as small overbite This explanation, however does not seem to apply to the present material, as cases with large adenoids and mouthbreathing have a tendency towards postnormal rather than prenormal occlusion Further studies seem necessary before an explanation can be found for the relationship shown

The skeleton variables for the relationship between upper anterior and total face height (A116) posterior face height (A94) and approximate vertical dimension of the body of the sphenoid bone (A127) appear to be of some importance as determinants of the size of overbite. The relationship between the regressand and these regressors is to be regarded as a parallel phenomenon rather than as a causal relationship

The regression equation also includes the variable for year of birth (A02) This is in line with the simple correlation analysis (cf Table

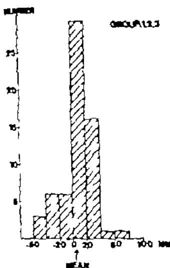




Fig. 34. Distribution of children in accordance with the *sagittal relationship between the mesial surfaces of the right first molars in the upper and lower jaws.* The distribution the same in the adenoidectomy group and the controls.

(5 p 56) which showed a highly significant correlation (= −0 40, $P < 0.001$) for the relationship between overbite and year of birth. These results fully agree with earlier reports by Seipel (1946), Baume (1950) and Moorees (1959) The increase in overbite with increasing age can be explained in terms of the difference in crown height between the deciduous and permanent incisors. Overbite involving the incisors thus increases in absolute terms from the deciduous to the permanent dentition but is not changed in relative terms (Moorees 1959) Approximately 35% of the children in this study had deciduous incisors.

No significant relationships were found for the airflow regressors in this regression analysis

Summary

This multiple regression analysis shows that a small overbite is common among children with crossbite or a tendency to crossbite, a small value for the relationship between anterior upper and total face height, and a small posterior upper face height. A small *overbite* was also found more frequently among the younger children

The size of overbite in the children in this study is considered to be a parallel phenomenon to crossbite or a tendency to crossbite and to the size of upper face height.

The increase in overbite with increasing age is considered to be a consequence of the difference in crown height between the deciduous and permanent incisors.

REGRESSAND SAGITTAL RELATIONSHIP BETWEEN MESIAL SURFACES OF UPPER AND LOWER RIGHT FIRST MOLARS

In the analysis presented in Table 45 the regressand was variable A57 Sagittal relationship between mesial surfaces of upper and lower right first molars, and the regressors were as follows: anamnesis variables A02–03 dentition variables A48, A55 airflow variables A67 A70 group variable A79 skeleton variables A85 A105 A113 tongue-position variable A1?9 The regressors were introduced in the following order A55 A113 A85 A105 and A03

The distribution of the control and adenoidectomy children with respect to the regressand is shown in Fig. 34

Table 45 *Regressand A57 Sagittal relation between the mesial surfaces of the right upper and lower first molars*

Regression coefficients, their std error level of significance (marked with asterisks), partial correlation coefficients, the total correlation coefficient (R^2) and the standard deviation of the residuals (R.S.D), in an analysis of 11 regressors

Regressor	Coefficient	Std. error	t value	Partial corr
Constant	33 4320	6.5187	5 13	—
A03 Sex	−1.0749	0 4374	−2.46	−0.22
A55 Overjet	−0.3645	0.1571	−2.32	−0.21
A85 n–s	−0.2629	0 0755	−3 48	−0.30
A105 ss–n–sm	−0 3133	0 1032	−3 03	−0.27
A113 lo–lo/n–gn	−0 1316	0.0462	−2.85	−0.25

$R^2 = 0.27$ R.S D = 2.29

Results

The regressors included in the regression equation as determinants of the sagittal relationship between the mesial surfaces of the upper and lower right first molars have a low coefficient of determination $R^2 = 0\ 27$ If one also includes *all the regressors enumerated above that* were not significant at the 5% level the coefficient of determination is increased to $R^2 = 0\ 30$

Variable A85 which represents the length of the anterior part of the cranial base appears to be the most important determinant in this regression analysis but has a very weak coefficient of determination by itself $R^2 = 0\ 05$ (cf Table 23 p 66) Since variables A85 and A57 both represent dimensions in the sagittal plane, the relationship obtained in this regression analysis can be interpreted as an example of a connection between skeleton and dentition variables in the same projection plane

The variable that displays the next strongest relationship with regressand A57 is A105 which represents the angle subspinale-nasion supramentale The relationship between the regressand and variable A113 Index for face width/face height indicates that children with high index values have a small sagittal distance i e a postnormal tendency between the mesial surfaces of the upper and lower right first molars

The sex variable (A03) displays an almost significant relationship with regressand A57 It was thus more common for the girls in this study to have a small sagittal distance between the mesial surfaces of the upper and lower right first molars, i e a tendency towards a postnormal molar relationship in the girls and/or a prenormal relationship in the boys.

The almost significant relationship between overjet (A55) and regressand A57 in this regression analysis corresponds to the relationship in the analysis with A55 as regressand.

A small sagittal distance i e a postnormal tendency between the mesial surfaces of the upper and lower right first molars, thus appears to be common among children with a large anterior cranial base length, large values for the angle subspinale nasion-supramentale large overjet large index values for face width/face height and among girls.

Discussion

In spite of the low coefficient of determination (R^2 0 27) one regressor displays highly significant relationships ($P < 0\ 001$) namely variable A85 while two are significant ($P < 0\ 01$) namely A105 and A113 The regressors A03 and A55 are almost significant (P 0 05) As is often the case with a low coefficient of determination the relationships between regressors and regressand are difficult to interpret.

A possible explanation for the correlations between variables A105 and A55 on the one hand and regressand A57 on the other is that

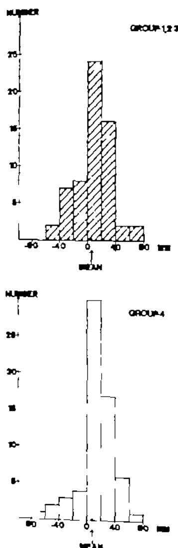


Fig 35 Distribution of children in accordance with the *sagittal relationship between the mesial surfaces of the left first molars in the upper and lower jaws.* The distribution is the same for the adenoidectomy group and the controls

a large sagittal difference in the anterior region is associated with a small difference in the sagittal plane between the mesial surfaces of the upper and lower first molars. This would be in line with the significant correlation described by Seipel (1946) between a postnormal molar relationship and increased overjet. This relationship should be interpreted, not as a causal connection between the regressors and the regressand, but as a parallel phenomenon.

Difficulty in measuring the regressand is sometimes responsible for a low coefficient of determination. In the present case, however the measurements were made on models and the error of method vis-à-vis the biological relationships is probably small. A possible explanation for the variations in the regressands is that certain variables have not been registered, e.g. mesial displacement of first molars as a result of premature loss of the deciduous molars

Summary

This multiple regression analysis suggests that a postnormal relationship between the mesial surfaces of the right first molars is common among children with a large anterior cranial base length, large values for the angle ss–n–sm, large overjet, large index values for face width/face height and among girls

As is often the case with a low coefficient of determination, the relationships between regressand and regressors are difficult to interpret. The almost significant relationship between a postnormal molar relationship and large overjet is nevertheless considered to be a parallel phenomenon.

REGRESSAND SAGITTAL RELATIONSHIP BETWEEN MESIAL SURFACES OF UPPER AND LOWER LEFT FIRST MOLARS

In the analysis presented in Table 46 the regressand was variable A58 Sagittal relationship between mesial surfaces of upper and lower left first molars, and the regressors were as follows: anamnesis variables A02–03 dentition variable A55 airflow variables A67 A70–group variable A79 skeleton variables A90 A106–107 tongue-position variable A129 Only one regressor A55 was introduced.

The distribution of the control and adenoidectomy children with respect to the regressand is shown in Fig. 35

Table 45 *Regressand A57 Sagittal relation between the mesial surfaces of the right upper and lower first molars*

Regression coefficients, their std error level of significance (marked with asterisks), partial correlation coefficients, the total correlation coefficient (R^2) and the standard deviation of the residuals (R.S.D) in an analysis of 11 regressors

Regressor	Coefficient	Std error	t value	Partial corr
Constant	33 4320	6.5187	5 13	—
A03 Sex	−1 0749	0.4374	−2.46	−0.22
A55 Overjet	−0.3645	0.1571	−2.32	−0.21
A85 n–s	−0.2629	0.0755	−3 48	−0.30
A105 ss–n–sm	−0.3133	0.1032	−3 03	−0.27
A113 lo–lo/n–gn	−0 1316	0.0462	−.85	−0.25

R^2 = 0.27 R.S.D = 2.29

Results

The regressors included in the regression equation as determinants of the sagittal relationship between the mesial surfaces of the upper and lower right first molars have a low coefficient of determination $R^2 = 0.27$ If one also includes all the regressors enumerated above that were not significant at the 5% level the coefficient of determination is increased to $R^2 = 0.30$

Variable A85 which represents the length of the anterior part of the cranial base, appears to be the most important determinant in this regression analysis but has a very weak coefficient of determination by itself $R^2 = 0.05$ (cf Table 23 p 66) Since variables A85 and A57 both represent dimensions in the sagittal plane the relationship obtained in this regression analysis can be interpreted as an example of a connection between skeleton and dentition variables in the same projection plane

The variable that displays the next strongest relationship with regressand A57 is A105 which represents the angle subspinale nasion-supramentale The relationship between the regressand and variable A113 Index for face *width/face height* indicates that children with high index values have a small sagittal distance i e a postnormal tendency between the mesial surfaces of the upper and lower right first molars

The sex variable (A03) displays an almost significant relationship with regressand A57 It was thus more common for the girls in this study to have a small sagittal distance between the mesial surfaces of the upper and lower right first molars, i e a tendency towards a postnormal molar relationship in the girls and/or a *prenormal relationship in the boys.*

The almost significant relationship between overjet (A55) and regressand A57 in this regression analysis corresponds to the relationship in the analysis with A55 as regressand

A small sagittal distance i e, a postnormal tendency between the mesial surfaces of the upper and lower right first molars, thus appears to be common among children with a large anterior cranial base length, large values for the angle subspinale-nasion supramentale large overjet large index values for face width/face *height and among girls*

Discussion

In spite of the low coefficient of determination ($R^2 = 0.27$) one regressor displays highly significant relationships ($P < 0.001$) namely variable A85 while two are significant ($P < 0.01$) namely A105 and A113 The regressors A03 and A55 are almost significant ($P < 0.05$) As is often the case with a low coefficient of determination the relationships between regressors and regressand *are difficult to interpret*

A possible explanation for the correlations between variables A105 and A55 on the one hand and regressand A57 on the other is that

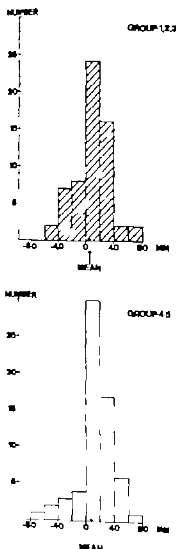


Fig. 35. Distribution of children in accordance with the *sagittal relationship between the mesial surfaces of the left first molars in the upper and lower jaws.* The distribution the same for the adenoidectomy group and the controls.

a large sagittal difference in the anterior region is associated with a small difference in the sagittal plane between the mesial surfaces of the upper and lower first molars. This would be in line with the significant correlation described by Serpel (1946) between a postnormal molar relationship and increased overjet. This relationship should be interpreted, not as a causal connection between the regressors and the regressand, but as a parallel phenomenon.

Difficulty in measuring the regressand is sometimes responsible for a low coefficient of determination. In the present case, however the measurements were made on models and the error of method vis-à-vis the biological relationships is probably small. A possible explanation for the variations in the regressands is that certain variables have not been registered, e.g. mesial displacement of first molars as a result of premature loss of the deciduous molars.

Summary

This multiple regression analysis suggests that a postnormal relationship between the mesial surfaces of the right first molars is common among children with a large anterior cranial base length, large values for the angle ss–n–sm, large overjet, large index values for face width/face height and among girls.

As is often the case with a low coefficient of determination, the relationships between regressand and regressors are difficult to interpret. The almost significant relationship between a postnormal molar relationship and large overjet is nevertheless considered to be a parallel phenomenon.

REGRESSAND: SAGITTAL RELATIONSHIP BETWEEN MESIAL SURFACES OF UPPER AND LOWER LEFT FIRST MOLARS

In the analysis presented in Table 46 the regressand was variable A58 Sagittal relationship between mesial surfaces of upper and lower left first molars, and the regressors were as follows: anamnesis variables A02–03 dentition variable A55 airflow variables A67 A70 group variable A79 skeleton variables A90, A106–107 tongue-position variable A129. Only one regressor A55 was introduced.

The distribution of the control and adenoidectomy children with respect to the regressand is shown in Fig. 35.

Table 45 *Regressand A57 Sagittal relation between the mesial surfaces of the right upper and lower first molars*

Regression coefficients, their std error level of significance (marked with asterisks), partial correlation coefficients, the total correlation coefficient (R^2), and the standard deviation of the residuals (R.S.D) *In an analysis of 11 regressors*

Regressor	Coefficient	Std. error	t value	Partial corr
Constant	33.4320	6.5187	5.13	—
A03 Sex	−1.0749	0.4374	−2.46	−0.[illegible]2
A55 Overjet	−0.3645	0.1571	−2.32	−0.21
A85 n–s	−0.[illegible]629	0.0755	−3.48	−0.30
A105 ss–n–sm	−0.3133	0.1032	−3.03	−0.27
A113 lo–lo/n–gn	−0.1316	0.0462	−2.85	−0.25

$R^2 = 0.27$ R.S.D = 2.29

Results

The regressors included in the regression equation as determinants of the sagittal relationship between the mesial surfaces of the upper and lower right first molars have a low coefficient of determination $R^2 = 0.27$ If one also includes all the regressors enumerated above that were not significant at the 5% level the coefficient of determination is increased to $R^2 = 0.30$

Variable A85 which represents the length of the anterior part of the cranial base appears to be the most important determinant in this regression analysis but has a very weak coefficient of determination by itself $R^2 = 0.05$ (cf *Table 23 p 66*) *Since variables A85 and A57* both represent dimensions in the sagittal plane, the relationship obtained in this regression analysis can be interpreted as an example of a connection between skeleton and dentition variables in the same projection plane.

The variable that displays the next strongest relationship with regressand A57 is A105 which represents the angle subspinale-nasion supramentale The relationship between the regressand and variable A113 Index for face width/face height indicates that children with *high index values have a small sagittal distance* i e a postnormal tendency between the mesial surfaces of the upper and lower right first molars

The sex variable (A03) displays an almost *significant relationship with regressand A57* It was thus more common for the girls in this study to have a small sagittal distance between the mesial surfaces of the upper and lower right first molars i e, a tendency towards a postnormal molar relationship in the girls and/or a prenormal relationship in the boys.

The almost significant relationship between overjet (A55) and regressand A57 in this regression analysis corresponds to the relationship in the analysis with A55 as regressand.

A small sagittal distance i e a postnormal tendency between the mesial surfaces of the upper and lower right first molars thus appears to be common among children with a large anterior cranial base length large values for the angle subspinale-nasion supramentale, large overjet large index values for face width/face height and among girls.

Discussion

In spite of the low coefficient of determination (R^2 0.27) one regressor displays highly significant relationships ($P < 0.001$) namely variable A85 while two are significant (P 0.01) namely *A105 and A113 The regressors A03 and* A55 are almost significant (P 0.05) As is often the case with a low coefficient of determination the relationships between regressors and regressand are difficult to interpret

A possible *explanation for the* correlations between variables A105 and A55 on the one hand and regressand A57 on the other is that

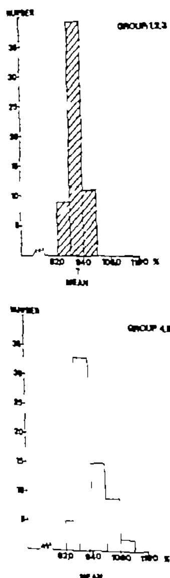


Fig 36 Distribution of children in accordance with the index values for the *relationship between the widths of the lower and upper arches between the first molars*. The distribution is the same for the adenoidectomy group and the controls.

gression analysis By itself, this variable has a coefficient of determination $R = 0.43$ (cf. Table 20, p 63) The relationship indicates that a wide lower arch in relation to the upper arch, i.e crossbite or a tendency to crossbite, tends to be accompanied by a small overbite

The next strongest relationship with the regressand is displayed by variable A96 Length of upper lip This relationship is positive and indicates that a long upper lip is common among children whose lower arch is wide in relation to the upper arch.

The regression analysis also indicates an almost significant relationship between mouth breathing (A15) and a narrow upper arch in relation to the lower arch.

Variable A92, Sagittal depth of bony nasopharynx, also shows some relation with the size of the index for lower and upper arch width between first molars.

Thus, the regression analysis shows that a narrow upper arch in relation to the lower arch, i.e crossbite or a tendency to crossbite, is common among children with a small overbite, long upper lip small sagittal depth of bony nasopharynx and mouth breathing.

Discussion

The regressors included in the regression equation as determinants of the index for lower and upper arch width between first molars comprise variables that express height dimensions in the dentition (A56) and face (A96) as well as variables for mouth breathing (A15) and size of nasopharynx (A92) A highly significant relationship is displayed for regressor A56 ($P < 0.001$)

The strong relationship between overbite (A56) and crossbite (A63) has already been interpreted as a parallel phenomenon (In the regression equation with A56 as regressand, p 102)

Variable A96 Height of upper lip can be said to represent variables associated with face height. As shown by the simple correlation analysis (cf Table 31 p 78), A96 correlates particularly strongly ($r = 0.61$ $P < 0.001$) with the variable for total face height (A88). The relationship between the present regressand and skeletal variables that express face height should be interpreted as a parallel phenomenon, in that high face height often occurs in

Table 46 *Regressand A58 Sagittal relation between the mesial surfaces of the left upper and lower first molars*

Regression coefficients, their std. error leve lof significance (marked with asterisks), partial correlation coefficients, the total correlation coefficient (R^2), and the standard deviation of the residuals (R.S.D) in an analysis of 10 regressors

Regressor	Coefficient	Std error	*t* value	Partial corr
Constant	2.9565	0.5318	5.59	—
A55 Overjet	−0.5827	0 1487	−3 91	−0.33

R^2 − 0 11 R.S D − 2.41

Results

Regressor A55 Overjet is included in the regression equation as a determinant of the sagittal relationship between the mesial surfaces of the upper and lower left first molars and gives a coefficient of determination of only $R^2 = 0\ 11$ The relationship for this regressor is highly significant ($P < 0\ 001$) If one also includes all the regressors enumerated above that are not significant at the 5% level, the coefficient of determination is increased only to $R^2 = 0\ 19$

The significant correlation between variable A55 and regressand A58 corresponds to the *almost significant relationship between A55* and regressand A57 in the preceding regression analysis

A small sagittal distance i e a postnormal tendency between the mesial surfaces of the upper and lower left first molars thus appears to be common among children with a large overjet

Discussion

The relationships demonstrated in the regression analysis with variable A57 as regressand can also be expected when the regressand is variable A58 though there may well be some difference between the variables in view of the local migration of teeth *that may have* occurred in the molar regions of either jaw on the right and left sides

REGRESSAND INDEX FOR LOWER AND UPPER ARCH WIDTHS BETWEEN FIRST MOLARS

In the analysis presented in Table 47 the regressand was *variable A63 Index for lower* and upper arch widths between first molars, and the regressors were as follows, anamnesis variables A02–04 A12–16 adenoid variables A20 A32 A35 A38 A40 dentition variables A48 A56 airflow variables A67 A70 A73 A76 group variable A79 skeleton variables A91–92, A96 A102, A121 A124 The regressors were introduced in the following order A56 A15 A96 and A92

The distribution of the control and adenoidectomy children with respect to the regressand is shown in Fig. 36

Results

The regressors included in the regression equation as determinants of the index for the relationship between lower and upper arch widths between first molars display a moderate coefficient of determination $R^2 = 0\ 38$ If one also includes all the above regressors that are not significant at the 5% level the coefficient of determination increases to $R^2 = 0\ 47$ The highly significant and the significant variables ($P < 0\ 001$ $P < 0\ 01$ respectively) display the *expected sign*

Variable A56 Overbite, displays the strongest relationship with the regressand in this re

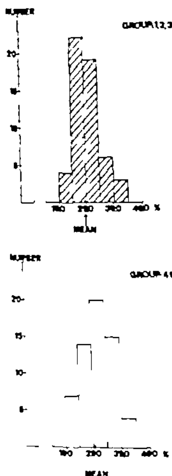


Fig 37 Distribution of children in accordance with the index values for the *relationship between height of palatal vault and width of upper arch between first molars*. The distribution is the same for the adenoidectomy group and the controls.

Z emer 195 Ballard & Gwynne Evans, 1958).

The opinion of Ricketts (1958 *b* 1968) that crossbite is often found in mouth breathers receives support from these results.

Summary

The multiple regression analysis shows that crossbite or a tendency to crossbite frequently occurs in children with a small overbite long upper lip small sagittal depth of nasopharynx and mouth breathing. All relationships between the regressand and the regressors are interpreted primarily as parallel phenomena, though a causal relationship between mouth breathing and the presence of crossbite is considered probable

REGRESSAND: INDEX FOR HEIGHT OF PALATAL VAULT AND UPPER ARCH WIDTH BETWEEN FIRST MOLARS

In the analysis presented in Table 48 the regressand was variable A66 Index for height of palatal vault and upper arch width between first molars, and the regressors were as follows. anamnesis variables A02–03 A05 A12, A15 dentition variable A61 airflow variables A67 A70 group variable A79 skeleton variables A80–81 A84 A86–90 A96–98 A100, A128 A113 interaction variable A67 × A15 The regressors were introduced in the following order: A02, A88 A15 A67 and A81

The distribution of the control and adenoidectomy children with respect to the regressand is shown in Fig. 37

Results

The regressors included in the regression equation as determinants of the index for height of palatal vault and upper arch width between first molars have a satisfactory coefficient of determination. $R^2 = 0.57$

The variable for year of birth (A02) appears to be the most important determinant in this regression analysis for the size of the index for height of palatal vault and upper arch width between first molars. By itself this variable has a coefficient of determination $R^2 = 0.38$ (cf Table 15 p 56) and is highly significant ($P < 0.001$)

The next strongest relationship with the regressand is displayed by the variable for mouth breathing (A15) but this is only significant at the 1% level ($P < 0.01$) The relationship indicates that children who breath through the mouth often have a high palatal vault and/or a narrow upper arch

Table 47 *Regressand A63 Relationship between lower and upper arch widths between first molars*

Regression coefficients, their std. error level of significance (marked with asterisks), partial correlation coefficients, the total correlation coefficent (R^2), and the standard deviation of the residuals (R.S D), in an analysis of 26 regressors

Regressor	Coefficient	Std. error	t value	Partial corr
Constant	91 7540	6.2360	14 72	—
A15 Mouth breathing	1 7958	0.8148	2.20	0.20
A56 Overbite	−1.5065	0.2807	−5.37	−0 44
A92 pm–ba	−0.2430	0.1132	−2.15	−0.19
A96 Height of upper lip	0.5428	0.1757	3 09	0.27

R^2 − 0.38 R.S.D − 4 03

conjunction with crossbite or a tendency to crossbite

The variable for mouth breathing (A15) also features in the regression equation as a determinant of the index for lower and upper arch width between first molars but is only significant at the 5% level It is probable that the determinative value of this variable also includes an influence from the adenoid, airflow and tongue-position variables. The simple correlation analyses demonstrated significant relationships between mouth breathing on the one hand and, on the other the adenoid variable A20 (r − 0 66 P < 0 001 cf Table 16 p 57) the preoperative airflow variable A67 (r − − 0 30 P < 0 001 cf Table 17 p 59) and the tongue position variable A129 (r − 0 47 P < 0 001 cf Table 19 p 62)

The relationship demonstrated in the regression equation between mouth breathing (A15) and crossbite (A63) has already been demonstrated in the simple correlation analysis (cf Table 15 p 56) It may be interpreted as a causal relationship and/or as reflecting a common underlying cause

A causal relationship between mouth breathing and the index for lower and upper arch width between first molars is envisaged as being due to the low position of the tongue in mouth breathing (cf Table 19 p 62) This enables the tongue to exert greater transverse pressure on the lower first molars than on the upper It is also conceivable that the obstruction of nose breathing tends to inhibit lateral growth of the upper face

Variable A92, Sagittal depth of nasopharynx, is also included as a regressor in this regression equation and is only significant at the 5% level. Considering that this variable displays strong significant correlations to the majority of skeleton variables that express nasopharyngeal dimensions (Table 31 p 78) it is conceivable that it features in the regression equation as a representative for these nasopharyngeal variables

The relationship demonstrated in the regression equation between the variable for sagittal depth of nasopharynx and the variable for crossbite can be interpreted as an expression of relationships between skeleton and dentition variables in neighbouring regions and is consequently to be regarded as indicating the same phenomenon.

The size of the index for lower and upper arch width between first molars in the children in this study is interpreted in this multiple regression analysis as a parallel phenomenon to skeleton variables representing face height and dimensions in the nasopharyngeal region and/or as a consequence of mouth breathing and the low tongue position associated with this

The results thus indicate that crossbite or a tendency to crossbite is often associated with a large face height and mouth breathing They therefore support the frequently expressed opinion that there is often an association between a narrow upper jaw a long narrow face and mouth breathing (e g. Brash 1929 Poncher Schour & Massler 1945 Emslie Massler &

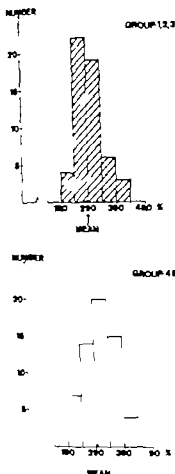


Fig 37 Distribution of children in accordance with the index for the *relationship between height of palatal vault and width of upper arch between first molars*. The distribution is the same for the adenoidectomy group and the controls.

Zwemer 195 Ballard & Gwynne-Evans, 1958).

The opinion of Ricketts (1958 b 1968) that crossbite is often found in mouth breathers receives support from these results

Summary

The multiple regression analysis shows that crossbite or a tendency to crossbite frequently occurs in children with a small overbite, long upper lip, small sagittal depth of nasopharynx and mouth breathing. All relationships between the regressand and the regressors are interpreted primarily as parallel phenomena, though a causal relationship between mouth breathing and the presence of crossbite is considered probable.

REGRESSAND· INDEX FOR HEIGHT OF PALATAL VAULT AND UPPER ARCH WIDTH BETWEEN FIRST MOLARS

In the analysis presented in Table 48 the regressand was variable A66, Index for height of palatal vault and upper arch width between first molars, and the regressors were as follows· anamnesis variables A02–03 A05 A12, A15 dentition variable A61 airflow variables A67 A70 group variable A79 skeleton variables A80–81 A84 A86–90 A96–98 A100, A128, A113 interaction variable A67 × A15 The regressors were introduced in the following order· A02 A88, A15 A67 and A81

The distribution of the control and adenoidectomy children with respect to the regressand is shown in Fig. 37

Results

The regressors included in the regression equation as determinants of the index for height of palatal vault and upper arch width between first molars have a satisfactory coefficient of determination. $R^2 = 0.57$

The variable for year of birth (A02) appears to be the most important determinant in this regression analysis for the size of the index for height of palatal vault and upper arch width between first molars. By itself this variable has a coefficient of determination $R^2 = 0.38$ (cf. Table 15 p 56) and is highly significant ($P < 0.001$)

The next strongest relationship with the regressand is displayed by the variable for mouth breathing (A15) but this is only significant at the 1% level ($P < 0.01$) The relationship indicates that children who breath through the mouth often have a high palatal vault and/or a narrow upper arch.

Table 48 *Regressand A66 Relationship between height of palatal vault and upper arch width between first molars*

Regression coefficients, their std. error level of significance (marked with asterisks), partial correlation coefficients, the total correlation coefficient (R^2), and the standard deviation of the residuals (R.S D), in an analysis of 4 regressors

Regressor	Coefficient	Std. error	t-value	Partial corr
Constant	152.5200	26.9712	5 65	—
A02 Year of birth	−2.6428	0.3366	−7 85	−0 60
A15 Mouth breathing	2.8349	1 0816	2.62	0.24
A67 Preop airflow before nose drops	0.2206	0 1024	2.15	0.20
A88 n–gn	0.2.26	0 1003	2.22	0.21

$R^2 = 0.57$ R.S.D = 5 05

The regression analysis also displays an almost significant relationship between nasal air flow preoperatively before nose drops (A67) and the regressand This relationship is positive, pointing to a large airflow for a high palatal vault and/or a narrow upper arch By including the interaction variable A67 × A15 it was found however that the relationship between A67 and regressand A66 only applies to the children who are nose breathers On the other hand, the airflow variable A67 appears to be of less importance for mouth breathers if one includes all the other regressors

The size of the index for height of palatal vault and upper arch width between first molars thus appears to depend in the first place on the age of the child

This regression analysis also shows that a high palatal vault and/or a narrow upper arch are frequently found in children who breath through the mouth

Discussion

The strong negative relationship between the regressand and year of birth suggests that the height of the palatal vault increases more with age than the width of the upper arch This has been demonstrated previously by Franke (1921) and Hellman (1927)

The presence of variable A15 Mouth breathing, as a regressor in this regression equation is to be regarded as a consequence of a high palate and/or a narrow upper arch rather than as a determinant of regressand A66 In this context, the relationship between arch width and mouth breathing is considered to be more relevant than that between height of palatal vault and mouth breathing (cf Table 15 p. 56) The relationship between mouth breathing and a narrow arch has already been discussed in connection with the regression analysis in which the regressand was variable A49 Upper arch width between first molars (see p 98)

The results in this regression analysis appear to support the opinion of several authors that children who breath through the mouth often have a narrow upper arch and/or a high palatal vault (e g Körbitz, 1910 Izard, 1925 Bowen & Balyeat, 1934 Massler Poncher & Schour 1945 Ballard, 1952)

Summary

This multiple regression analysis shows that the size of the index for height of palatal vault and upper arch width between first molars is primarily dependent on the age of the child It also shows that a high palatal vault and/or a narrow upper arch are often found in mouth breathers Mouth breathing in these children is to be regarded as a consequence of a high palatal vault and or a narrow upper arch rather than as a cause of this In this context the relationship between arch width and mouth breathing is considered more relevant than that between height of palatal vault and mouth breathing.

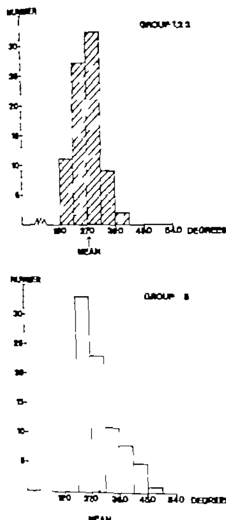


Fig 38 Distribution of children by the size of the angle ML/NL The difference between the means for the adenoidectomy group and the controls is entirely ascribable to the high values in adenoidectomy group 5 It is also worth noting that the control group displays symmetric distribution, whereas that for the adenoidectomy children J-shaped.

REGRESSAND- ANGLE BETWEEN MANDIBULAR AND NASAL LINES

In the analysis presented in Table 49 the regressand was variable A107 Angle between mandibular and nasal lines, and the regressors were as follows: anamnesis variables A02, A05–06 A08, A1 –16 adenoid variables A20 A29 A32, A38 A40 dentition variables A49 A56 group variable A79 airflow variables A67 A70 A73 A76 skeleton variables A85 A87 A92–93 A96–97 A103 A105 A109 A124 A126 The regressors were introduced in the following order A96 A105 A97 A70 A124 and A85

The distribution of the control and adenoidectomy children with respect to the regressand is shown in Fig. 38

Results

The regressors included in the regression equation as determinants of the angle between the mandibular and nasal lines have a moderate coefficient of determination. $R^2=0.45$ If one also includes all the above regressors that are not significant at the 5% level, the coefficient of determination rises to $R^2=0.63$

Variable A105 which represents the angle subspinale-nasion-supramentale, features in this regression analysis as the most important determinant but, by itself has a very low coefficient of determination. $R^2=0.04$ (cf. Table 31 p 78)

The next strongest relationship with the regressand is displayed by the variable for the angle subspinale-nasion-basion (A124)

The variables for height of upper (A96) and lower lip (A97) are also included as regressors, as is the variable for the length of the anterior part of the cranial base (A85)

Airflow variables as determinants of the size of the regressand are represented in this regression equation by variable A70

According to this multiple regression analysis, a large angle between the mandibular and nasal lines frequently occurs in children with a large angle ss–n–sm, a small angle ss–n–ba, long upper and lower lips, a short anterior cranial base and small nasal airflow

Discussion

All the regressors in the regression equation are highly significant ($P<0.001$) with the exception of the airflow variable (A70)

Table 48 *Regressand A66 Relationship between height of palatal vault and upper arch width between first molars*

Regression coefficients, their std. error level of significance (marked with asterisks), partial correlation coefficients, *the total correlation coefficient (R^2) and the standard deviation of the residuals (R.S.D), in an analysis of 24 regressors*

Regressor	Coefficient	Std. error	*t* value	Partial corr
Constant	152.5200	26.9712	5 65	—
A02 Year of birth	−.6428	0.3366	−7.85	−0.60
A15 Mouth breathing	2.8349	1 0816	2.62	0.24
A67 Preop airflow before nose drops	0.2206	0.1024	2.15	0.20
A88 n–gn	0.2226	0.1003	2.22	0.21

R^2 = 0.57 R.S D − 5 05

The regression analysis also displays an almost significant relationship between nasal air flow preoperatively before nose drops (A67) and the regressand This relationship is positive pointing to a large airflow for a high palatal vault and/or a narrow upper arch By including the interaction variable A67 × A15 it was found however that the relationship between A67 and regressand A66 only applies to the children who are nose breathers. On the other hand the airflow variable A67 appears to be of less importance for mouth breathers if one includes all the other regressors

The size of the index for height of palatal vault and upper arch width between first molars thus appears to depend in the first place on the age of the child

This regression analysis also shows that a high palatal vault and/or a narrow upper arch are frequently found in children who breath through the mouth

Discussion

The strong negative relationship between the regressand and year of birth suggests that the height of the palatal vault increases more with age than the width of the upper arch This has been demonstrated previously by Franke (1921) and Hellman (1927)

The presence of variable A15 Mouth breathing, as a regressor in this regression equation is to be regarded as a consequence of a high palate and/or a narrow upper arch rather than as a determinant of regressand A66 In this context, the relationship between arch width and mouth breathing is considered to be more relevant than that between height of palatal vault and mouth breathing (cf Table 15 p 56) The relationship between mouth breathing and a narrow arch has already been discussed in connection with the regression analysis in which the regressand was variable A49 Upper arch width between first molars (see p 98)

The results in this regression analysis appear to support the opinion of several authors that children who breath through the mouth often have a narrow upper arch and/or a high palatal vault (e g. Körbitz, 1910 Izard 1925 Bowen & Balyeat, 1934 Massler Ponchcr & Schour 1945 Ballard 1952)

Summary

This multiple regression analysis shows that the size of the index for height of palatal vault and upper arch width between first molars is primarily dependent on the age of the child It also shows that a high palatal vault and/or a narrow upper arch are often found in mouth breathers Mouth breathing in these children is to be regarded as a consequence of a high palatal vault and or a narrow upper arch rather than as a cause of this. In this context the relationship between arch width and mouth breathing is considered more relevant than that between height of palatal vault and mouth breathing

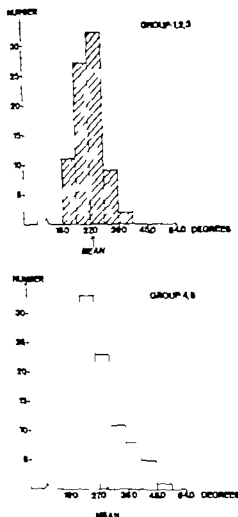


Fig. 38. Distribution of children by the size of the angle *ML/NL*. The difference between the means for the adenoidectomy group and the controls is entirely ascribable to the high values in adenoidectomy group 5. It is also worth noting that the control group displays symmetric distribution, whereas that for the adenoidectomy children is J-shaped.

REGRESSAND: ANGLE BETWEEN MANDIBULAR AND NASAL LINES

In the analysis presented in Table 49 the regressand was variable A107 Angle between mandibular and nasal lines, and the regressors were as follows: anamnesis variables A02, A05–06, A08 A12–16 adenoid variables A20 A29 A32, A38 A40 dentition variables A49 A56 group variable A79 airflow variables A67 A70, A73 A76 skeleton variables A85 A87 A92–93 A96–97 A103 A105 A109 A124 A126 The regressors were introduced in the following order: A96, A105 A97 A70 A124 and A85

The distribution of the control and adenoidectomy children with respect to the regressand is shown in Fig. 38

Results

The regressors included in the regression equation as determinants of the angle between the mandibular and nasal lines have a moderate coefficient of determination: $R^2 = 0.45$ If one also includes all the above regressors that are not significant at the 5% level the coefficient of determination rises to $R^2 = 0.63$

Variable A105 which represents the angle subspinale-nasion-supramentale, features in this regression analysis as the most important determinant but, by itself has a very low coefficient of determination: $R^2 = 0.04$ (cf Table 31 p 78)

The next strongest relationship with the regressand is displayed by the variable for the angle subspinale-nasion-basion (A124)

The variables for height of upper (A96) and lower lip (A97) are also included as regressors, as is the variable for the length of the anterior part of the cranial base (A85)

Airflow variables as determinants of the size of the regressand are represented in this regression equation by variable A70

According to this multiple regression analysis, a large angle between the mandibular and nasal lines frequently occurs in children with a large angle ss–n–sm, a small angle ss–n–ba, long upper and lower lips, a short anterior cranial base, and small nasal airflow

Discussion

All the regressors in the regression equation are highly significant ($P < 0.001$) with the exception of the airflow variable (A70)

Table 49 *Regressand A107 Angle between mandibular and nasal lines*

Regression coefficients, their std. error level of significance (marked with asterisks), partial correlation coefficients, the total correlation coefficient (R^2), and the standard deviation of the residuals (R.S.D), in an analysis of 32 regressors

Regressor	Coefficient	Std. error	t-value	Partial corr
Constant	56.9900	10.8710	5.24	—
A70 Preop airflow after nose drops	−0.1377	0.0536	−2.57	−0.20
A85 n–s	−0 4088	0.1163	−3.51	−0.27
A96 Height of upper lip	0.5928	0 1605	3 69	0.28
A97 Height of lower lip	0.4051	0.0989	4 10	0.31
A105 ss–n–sm	0.8107	0 1624	4 99	0.37
A124 ss–n–ba	−0 4575	0 1089	−4.20	−0.31

R^2 − 0.45 R.S.D − 4 19

The relationships obtained between the regressand and regressors A85 Anterior cranial base length A105 Angle ss–n–sm and A124 Angle ss–n–ba, may be regarded as indicators of the same facial morphology The negative relationship between the angle ss–n–ba (A124) and the angle between the mandibular and nasal lines (A107) agrees with descriptions of individuals with small values for the angles s–n–ss and s–n–sm (Björk 1947 Lindegård 1953 Solow 1966 Hasund & Remme 1967)

The relationship between preoperative air flow (A70) and the regressand can be interpreted in part as a reflection of the same underlying cause and in part as an expression for a causal connection

The latter interpretation reflects the view that the determinative value of A70 probably includes influences from variables for mode of breathing and adenoids as well as the consideration that posterior rotation of the lower jaw is facilitated in mouth breathers. It has been pointed out by Ricketts (1968) that such posterior rotation occurs in mouth breathers because they often hold the head tilted slightly backwards.

Summary

This multiple regression analysis shows that a large angle between the mandibular and nasal lines is often found in children with a large angle ss–n–sm a small angle ss–n–ba long

Table 50 *Stepwise regression analysis Regressand A46 Angle between upper incisors and nasion-sella line*

Regression coefficients, their std error level of significance, partial correlation coefficients, the total correlation coefficient (R^2), and the standard deviation of the residuals (R.S.D), in an analysis of 3 regressors introduced in the following order A 32 Size of adenoids A15 Mouth breathing A129 Tongue position Each step is shown separately

Step	Regressor	Coefficient	Std. error	t value	Partial corr
1	Constant	116.7000	4 9818	23.42	
	A32 Size of adenoids	0 1499	0 0601	−2.50	−0.34
	R^2 0 11 R.S.D − 6.09				
	Constant	106 8400	8 4917	1..58	
	A32 Size of adenoids	0 1286	0.2042	0.63	0.09
	A15 Mouth breathing	− 8.3832	5 8790	− 1 43	−0.20
	R^2 − 0.15 R.S.D − 6.03				
3	Constant	103.2400	8.6187	11 98	
	A3 Size of adenoids	0 1533	0.2011	0 76	0 11
	A15 Mouth breathing	− 10.3420	5 8940	− 1 75	−0.25
	A129 pm–t	0.4402	0.2663	1 65	0.24
	R^2 − 0.20 R.S.D − 5 92.				

Table 51 *Stepwise regression analysis. Regressand. A48, Angle between lower incisors and mandibular line*

Analyses analogous with that reported in Table 50

Step	Regressor	Coefficient	Std. error	t-value	Partial corr
1	Constant	115.2200	5.0405	22.86	
	A32 Size of adenoids	−0.3078	0.0603	−5 10	−0.59
	R^2 0.35 R.S.D 6.05				
2	Constant	104 7100	8.5496	12.25	
	A32 Size of adenoids	−0.0144	0.2031	0.07	−0 01
	A15 Mouth breathing	−8.7687	5.8022	−1.51	−0.22
	R^2 0 38 R.S.D. 5.97				
3	Constant	105 2300	8.8330	11 91	
	A32 Size of adenoids	−0.0164	0.2052	−0.08	−0 01
	A15 Mouth breathing	−8.4697	5.9558	−1 42	−0.21
	A129 pm–t	−0.0776	0.2762	−0.28	−0 04
	R^2 0.38 R.S.D = 6 03				

upper and lower lips, short anterior cranial base and small nasal airflow

The relationships obtained between the regressand and the regressors are considered to have the same underlying mechanism, though a causal connection may be expressed to some extent by the relationship between the regressand and the airflow variable. A large angle between the mandibular and nasal lines in children with a small nasal airflow is explained in this context by the circumstance that posterior rotation of the lower jaw is facilitated in mouth breathers.

ANALYSIS OF THE IMPORTANCE OF TONGUE POSITION FOR CERTAIN DENTITION VARIABLES

The simple correlation analyses showed that there are significant correlations between mouth breathing and large adenoids on the one hand and, on the other the dentition variables A46 Angle between upper incisors and nasion-sella line, A48, Angle between lower incisors and mandibular line, and A49 Upper arch width between first molars cf Tables 15 and 21 pp 56 and 64

A separate analysis has therefore been made to investigate whether the relationship between adenoids and these dentition variables can be attributed to the presence of adenoids causing mouth breathing, which leads in turn to a change in tongue position that then affects these dentition variables

The analysis was made on 51 of the children in the present study selected as having small or extremely large adenoids. The group with small adenoids comprised the controls whose size of adenoids according to variable A32 was less than the mean for the controls in group 1 i.e A32 < 73 64 % (cf. Table 10 p. 45) The group with extremely large adenoids comprised the adenoidectomy children whose corresponding value for variable A32 was greater than the mean for the adenoidectomy children in group 5 i.e. A32 > 91 19 % (cf. Table 10 p 45)

Regression analyses were performed with one of the dentition variables mentioned above as regressand. The regressors were variables for mouth breathing (A15), size of adenoids (A32) and tongue position (A129).

The regression analyses were performed with a stepwise procedure, the variable for size of adenoids (A32) being introduced first, followed by the variable for mouth breathing (A15) and

Table 49 *Regressand A107 Angle between mandibular and nasal lines*

Regression coefficients, their std. error level of significance (marked with asterisks), partial correlation coefficients, the total correlation coefficient (R^2), and the standard deviation of the residuals (R.S.D), in an analysis of 32 regressors

Regressor	Coefficient	Std. error	t value	Partial corr
Constant	56.9900	10 8710	5.24	—
A70 Preop airflow after nose drops	−0.1377	0 0536	−2.57	−0.20
A85 n–s	−0 4088	0.1163	−3.51	−0.27
A96 Height of upper lip	0.5928	0 1605	3 69	0.28
A97 Height of lower lip	0 4051	0.0989	4 10	0.31
A105 ss–n–sm	0 8107	0 1624	4 99	0.37
A124 ss–n–ba	−0 4575	0 1089	−4.20	−0.31

R^2 = 0 45 R.S D = 4 19

The relationships obtained between the regressand and regressors A85 Anterior cranial base length A105 Angle ss–n–sm and A124 Angle ss–n–ba, may be regarded as indicators *of the same facial morphology The negative* relationship between the angle ss–n–ba (A124) and the angle between the mandibular and nasal lines (A107) agrees with descriptions of individuals with small values for the angles s–n–ss and s–n–sm (Björk 1947 Lindegård, 1953 Solow 1966 Hasund & Remme 1967)

The relationship between preoperative air flow (A70) and the regressand can be interpreted in part as a reflection of the same underlying cause and in part as an expression for a causal connection

The latter interpretation reflects the view that the determinative value of A70 probably includes influences from variables for mode of breathing and adenoids as well as the consider*ation that posterior rotation of the lower jaw* is facilitated in mouth breathers It has been pointed out by Ricketts (1968) that such posterior rotation occurs in mouth breathers because they often hold the head tilted slightly backwards

Summary

This multiple regression analysis shows that a large angle between the mandibular and nasal lines is often found in children with a large angle ss–n–sm a small angle ss–n–ba long

Table 50 *Stepwise regression analysis Regressand. A46 Angle between upper incisors and nasion-sella line*

Regression coefficients, their std. error level of significance, partial correlation coefficients, the total correlation coefficient (R^2), and the standard deviation of the residuals (R.S.D), in an analysis of 3 regressors introduced in the following order A32, Size of adenoids, A15 Mouth breathing, A129 Tongue position. Each step is shown separately

Step	Regressor	Coefficient	Std error	t value	Partial corr
1	Constant	116.7000	4 9818	23 42	
	A32 Size of adenoids	0 1499	0 0601	−2.50	−0.34
	R^2 = 0 11 R.S D = 6 09				
2	Constant	106.8400	8 4917	12.58	
	A32 Size of adenoids	0.1286	0 2042	0 63	0 09
	A15 Mouth breathing	−8.3832	5 8790	1 43	−0.20
	R^2 = 0 15 R.S.D = 6 03				
3	Constant	103.2400	8 6187	11 98	
	A32 Size of adenoids	0.1533	0.2011	0.76	0.11
	A15 Mouth breathing	−10.3420	5 8940	−1 75	−0.25
	A129 pm–t	0 4402	0.2663	1 65	0.24
	R^2 = 0.20 R.S D = 5 92.				

Table 51 *Stepwise regression analysis. Regressand A48 Angle between lower incisors and mandibular line*

Analysis analogous with that reported in Table 50

Step	Regressor	Coefficient	Std. error	t-value	Partial corr
1	Constant	115.2200	5.0405	22.86	
	A32 Size of adenoids	−0.3078	0.0603	−5.10	−0.59
	R^2 0.35 R.S.D 6.05				
2	Constant	104 7100	8.5496	12.25	
	A32 Size of adenoids	−0.0144	0 2031	0 07	−0 01
	A15 Mouth breathing	−8.7687	5.8022	1.51	−0.22
	R^2 0.38, R.S.D. 5.97				
3	Constant	105.2300	8.8330	11.91	
	A32 Size of adenoids	−0.0164	0.2052	−0.08	−0.01
	A15 Mouth breathing	−8.4697	5.9558	−1 42	−0.21
	A129 pm–t_t	0.0776	0.2762	−0.28	−0 04
	R^2 0.38 R.S D 6 03.				

upper and lower lips, short anterior cranial base and small nasal airflow

The relationships obtained between the regressand and the regressors are considered to have the same underlying mechanism, though a causal connection may be expressed to some extent by the relationship between the regressand and the airflow variable. A large angle between the mandibular and nasal lines in children with a small nasal airflow is explained in this context by the circumstance that posterior rotation of the lower jaw is facilitated in mouth breathers.

ANALYSIS OF THE IMPORTANCE OF TONGUE POSITION FOR CERTAIN DENTITION VARIABLES

The simple correlation analyses showed that there are significant correlations between mouth breathing and large adenoids on the one hand and, on the other the dentition variables A46 Angle between upper incisors and nasion-sella line, A48, Angle between lower incisors and mandibular line, and A49 Upper arch width between first molars cf Tables 15 and 21 pp 56 and 64

A separate analysis has therefore been made to investigate whether the relationship between adenoids and these dentition variables can be attributed to the presence of adenoids causing mouth breathing, which leads in turn to a change in tongue position that then affects these dentition variables

The analysis was made on 51 of the children in the present study selected as having small or extremely large adenoids. The group with small adenoids comprised the controls whose size of adenoids according to variable A32 was less than the mean for the controls in group 1 i.e. A32 < 73 64 % (cf. Table 10 p 45) The group with extremely large adenoids comprised the adenoidectomy children whose corresponding value for variable A32 was greater than the mean for the adenoidectomy children in group 5 i.e. A32 > 91 19 % (cf. Table 10 p 45)

Regression analyses were performed with one of the dentition variables mentioned above as regressand. The regressors were variables for mouth breathing (A15) size of adenoids (A32) and tongue position (A129)

The regression analyses were performed with a stepwise procedure, the variable for size of adenoids (A32) being introduced first, followed by the variable for mouth breathing (A15) and

Table 52. *Stepwise regression analysis Regressand. A49 Upper arch width between first molars*
Analysis analogous with that reported in Table 50

Step	Regressor	Coefficient	Std. error	*t* value	Partial corr
1	Constant	47.5420	1 8241	26.06	
	A32 Size of adenoids	−0.0322	0.0219	−1 47	−0.21
	R^2 = 0.04 R.S.D = 2.16				
2	Constant	51 7300	3 1771	16.28	
	A32 Size of adenoids	−0 1472	0 0752	−1 96	−0.27
	A15 Mouth breathing	3.3915	2.1230	15 98	0.23
	R^2 = 0.09 R.S.D = 2.14				
3	Constant	51 6790	3.3104	15 61	
	A12 Size of adenoids	−0 1468	0 0762	−1 93	−0.27
	A15 Mouth breathing	3.3619	2.1966	1.53	0.[illegible]2
	A129 pm–t	0.0063	0 1005	0 06	0 01
	R^2 = 0.09 R.S.D = 2.16.				

then the variable for tongue position (A129) The results of the three stages are shown in Tables 50 51 and 52

Since the groups are comparatively small true relationships will be more difficult to demonstrate in these analyses than in those involving all the children

In the case of the variable for tongue position (A129) none of the analyses demonstrated any significant regression coefficients

In the case of the dentition variables A46 Angle between upper incisors and nasion-sella line, and A48 Angle between lower incisors and mandibular line, the regression analyses indicate that the relationship between size of adenoids and these dentition variables is established via mouth breathing

In the case of dentition variable A49 Upper arch width between first molars, no such indication is detectable in the regression analysis

No support has been obtained for the hypothesis that the relationship between these dentition variables (A46, A48 and A49) on the one hand and size of adenoids and mouth breathing on the other can be attributed to tongue position.

These observations refer to conditions before adenoidectomy The question could be tackled better however if these initial observations were combined with conditions one year *after adenoidectomy* since this operation can be expected to affect size of adenoids, mode of breathing and tongue position and consequently one would expect to find a change in the dentition If the causal mechanism suggested above does in fact exist

Number of observed and expected significant analyses at the 5 %, 1 % and 0.1 % levels

A total of 17 024 analyses of significance have been performed in this study and of these, 2255 proved to be significant at the 0.1% level, 3427 at the 1% level and 4988 at the 5% level. Assuming all differences to be due to chance, the hypothetical number of expected significant analyses amounts to 0.001 × 17,024 = 17.0 at the 0.1% level, 0.01 × 17,024 = 170.2 at the 1% level and 0.05 × 17,024 = 851.0 at the 5% level.

From this it can be seen that a considerable proportion of the significant results obtained at the 5% level, namely (0.05 × 17 024)/4988 = 17.1% can be suspected of being artefacts. Conclusions concerning differences, correlation coefficients and regression coefficients at the 5% level should therefore be regarded with caution.

At the 1% level, however the number of artefact relationships and differences amounts

Table 53 *The hypothetical number of expected significant variables (assuming all differences to be due to chance) at the three levels of significance in relation to the observed number of significant variables*

		Level of significance								
		0.1			1			5		
		Observed	Expected	Expect./Observ	Observed	Expected	Expect./Observ	Observed	Expected	Expect./Observ %
Differences between means	Total number of differences obtained									
	1333	142	1.3	0.9	236	13.3	5.6	394	66.6	16.9
Sample correlation analyses	Total number performed									
	15,225	2077	15.2	0.7	3137	152.2	4.9	4526	761.2	16.7
Multiple regression analyses	Total number performed									
	466	31	0.5	1.6	45	4.6	10.2	67	23.0	34.3
Differences, correlation analyses and regression analyses	Total number									
	17,024	2255	17.0	0.8	3427	170.2	4.9	4988	851.0	17.1

to no more than approximately 5% (4 9%) which is a risk one should be prepared to take. At the 0 1% level the corresponding incidence of artefact relationships and differences is rather less than 1% (0 8%) which is to be regarded as fully acceptable

Summing up it can be noted that the detailed discussion of correlation coefficients, regression coefficients and differences is only justified for values at the 1% and 0 1% levels of significance These findings serve to explain the scarcity of comments in the present study concerning relationships and differences at the 5% level

Frequency of adenoid facies as assessed from photographs

Results

The numerical and percentage frequences of so-called adenoid facies (see Fig. 3 p 16) as assessed from photographs by an orthodontist and an otologist are presented in Table 54 Such assessments were made for all the 81 children in the adenoidectomy group and 77 of the controls (no photograph was available for the other 4 controls)

It will be seen from the table that the frequency of so-called adenoid facies is considerably higher among the adenoidectomy children than the controls. The difference is highly significant ($P < 0.001$)

There is good agreement between the two observers assessments. Judging from the cases which both observers assessed in the same way the frequency of adenoid facies in the present study amounted to 25.9% in the group of children who underwent adenoidectomy Only one of these children belonged to group 4 i.e adenoidectomy as a result of recurrent otitis media.

Adenoid facies was also noted in about 4% of the control children. Only one of these controls belonged to group 3 i.e. the control group for children with large radiographic size of adenoids but no clinical breathing discomfort.

Discussion

Of the children with enlarged adenoids who underwent adenoidectomy only about one in four presented so-called adenoid facies. More over this facial type was registered in some, albeit only a few of the controls. In an un selected study however one would expect to find a larger number of children with so-called adenoid facies than in the present control group, since a number of adenoidectomy cases would be included in an unselected series.

Table 54 *Frequence of children with so called adenoid facies in the adenoidectomy group and the control group as assessed independently by two observers*

The figures in brackets show the number of children who were classified in the same way by both observers

Observer	Adenoid facies in adenoidectomy group		Adenoid facies in controls	
Orthodontist	28 (21)	34.5 (25.9)	4 (3)	5.0 (3.9)
Otologist	25 (21)	30.9 (25.9)	6 (3)	7.8 (3.9)

General discussion and conclusions

CONCERNING THE EFFECT OF ADENOIDS ON MODE OF BREATHING AND NASAL AIRFLOW AND THEIR RELATIONSHIP TO CHARACTERISTICS OF THE FACIAL SKELETON AND THE DENTITION

Is there a causal connection between adenoids and mouth breathing?

The influence of adenoids on the mode of breathing has been variously assessed in the literature but it seems to be generally agreed *that they may be a contributory cause of* mouth breathing. It has even been asserted for instance by Brash (1929) Neivert (1939) Cooke (1940) Leech (1958) Moyers (1963) and Reed (1963) that adenoids are the primary cause of mouth breathing.

In children with adenoids the relationship between their size and the size of the nasopharynx has been cited as a decisive factor for oral or nasal breathing by Siebenmann (1897) Nordlund (1918) Bernfeld (1927) Brash (1929) Schüller (1929) Emslie, Massler & Zwemer (1952) Ricketts (1954) Subtelny (1954) Goldman & Bachman (1958) and Lubarth (1960)

The present study has shown that a relationship exists between size of adenoids and mouth breathing In the multiple regression analysis with mouth breathing as the dependent variable (see p 84) the variable for size of adenoids gave a high coefficient of determination ($R^2 = 0.70$) by itself and this was further increased when the variable for size of nasopharynx was also introduced

That the size of the nasopharyngeal airway is important for the mode of breathing has been demonstrated in Fig. 24 (p 86) which shows that mouth breathers comprise 93% (41 out of 44 children) of the group with a small nasopharyngeal passage (zone I) but only 5% (4 out of 76 children) of the group with a large passage (zone II) The diagram also shows that a small nasopharynx combined with small adenoids is only occasionally accompanied by mouth breathing. Similarly even children with large adenoids may have an adequate air passage if the nasopharynx is also large Such children are consequently not obliged to resort to mouth breathing.

The present results provide no direct indication of the population incidence of mouth breathing as caused by adenoids combined with *a small nasopharyngeal airway* Compared with the total population the adenoidectomy group is overrepresented in relation to the controls.

Another finding of interest is that size of adenoids according to the clinical assessment displays almost the same correlation with mouth breathing as size of adenoids measured on lateral cephalometric radiographs

The relationships obtained warrant the conclusion that adenoids lead to mouth breathing primarily in children with a small nasopharynx. *In these children therefore adenoidectomy is especially indicated as a means of promoting a change to nasal breathing*

How is nasal airflow influenced by adenoids?

In order to obtain an objective picture of the passage of air through the nasopharynx recordings were made of nasal airflow in lit/min.

The results show that nasal airflow is low in children with large adenoids and high in those with small or no adenoids (cf Fig. 25 p 87) *and that the size of nasal airflow is* essentially determined by the relationship between *size of adenoids and size of nasopharynx*

It is also shown that the nasal airflow increases after adenoidectomy

Objective recordings of nasal airflow to elucidate its relationship with size of adenoids have earlier been described by Stoksted (1951) and Linder Aronson & Bäckström (1960)

The present results show that size of adenoids is decisive for the rate of nasal airflow only in children with very large adenoids. This implies that the size of the nasopharynx is of little importance for nasal airflow if the adenoids are so large that they severely impede or entirely obstruct the passage of air The size of the nasopharynx is also of little account for nasal airflow if there are no adenoids because the passage of air is then adequate regardless of the size of the nasopharynx. It is chiefly in children with small or moderate adenoids that the size of the nasopharynx is of essential importance for nasal airflow The effect of small or moderate adenoids on nasal airflow will accordingly vary with the size of the nasopharynx. Even children with small adenoids may thus have a low nasal airflow if the nasopharynx is also small. Particular attention should therefore be paid to the size of the nasopharynx when assessing the indications for adenoidectomy

It is remarkable that although the correlations between adenoids and mouth breathing and adenoids and airflow are comparatively strong (0 66, −0 45 respectively), the correlation between mouth breathing and airflow is rather weak (−0.30) From this it must be concluded, like Rasmus & Jacobs (1969) that assessments of mode of breathing cannot be regarded as an acceptable substitute for measurements of nasal airflow and vice versa. This serves to emphasize the diagnostic importance of airflow measurements according to the present method as a means of demonstrating an impaired nose breathing capacity—even in cases where the mode of breathing has been established

The present study thus provides an objective picture of the impaired function in the [illegible] nce of adenoids.

Concerning the secondary effects of nasal obstruction a good deal of research has been conducted on the lower respiratory airways. It has been found by Lüscher (1930) that the stimulus produced by air currents on the trigeminal nerves in the nasal mucous membrane played an important part in the movement of the thorax-lung system by reflex action. Furthermore, like Sercer (1930) and Kreewinsch (1932), he reported disturbance of the acid-base balance in the blood of patients with nasal obstruction and suggested that this might be due to reduced pulmonary ventilation.

This question has attracted renewed attention in recent years as a result of extensive investigations by Ogura et al. (1964 1966, 1968 *a*, *b*) Togawa et al. (1966) and Unno et al. (1968) who have investigated the influence of nasal obstruction on pulmonary mechanics. In successive studies they observed decreased elasticity of the lungs and increased pulmonary (airway and tissue) resistance in 97 subjects with relatively high nasal obstruction. These changes were observed during mouth breathing as well as nasal breathing and were directly related to the degree of nasal obstruction. The authors suggest that the changes in pulmonary function are reversible and probably caused by way of a reflex action.

Chronic upper airway obstruction as a new and previously unrecognized cause of heart failure was first presented by Menasche et al. (1965) Soon thereafter Noonan (1965) described two cases of reversible cor pulmonale due to hypertrophy of tonsils and adenoids. Luke et al. (1966) have reported four patients with severe nasopharyngeal obstruction who presented cardio-respiratory complications ranging from moderate cardial enlargement and right ventricular hypertrophy to cor pulmonale and pulmonary edema. Improvement following tonsillectomy and adenoidectomy was impressive.

A causal connection between chronic nasopharyngeal obstruction on the one hand and hypoventilation and cor pulmonale on the other has been described in a total of four cases by

Levy et al. (1967) Pilapil et al (1967) and Massumi et al (1969) In all these cases, adenoidectomy or tonsillectomy was followed by substantial improvement.

Even if the number of published cases with severe pulmonary and cardiac changes due to chronic nasopharyngeal obstruction is small in relation to all the children who experience discomfort from adenoids, it is conceivable that the lower respiratory airways are affected to some extent in many young children with nasal obstruction Considering that the reported changes appear to be reversible early diagnosis is called for and relief of the obstruction As indicated by the results of the present study the objective registration of nasal airflow is an important diagnostic aid for evaluating nasal respiration Indirectly the results also provide further evidence of the value of generous indications for adenoidectomy particularly in children with a small nasopharynx.

Is there a connection between adenoids and so-called adenoid facies?

The question whether adenoids are associated with a special facial type known as adenoid facies has been discussed ever since Meyer (1868) drew attention to the deleterious effect of adenoids on the hearing as well as on the general condition of the growing child It has been asserted on the one hand that adenoids combined with mouth breathing lead to special facial characteristics (e g Körner 1891 Cooke 1940 McCoy 1941 Massler Poncher & Schour 1945 Negus, 1955 Moyers, 1963) and, on the other that this combination has no such effect (e g. Kingsley 1888 Siebenmann 1897 Whitaker 1911 Nordlund, 1918 Brash 1929 Ballard, 1957 and Tulley 1966)

In the present study photographs of the children were judged independently by two observers and it was found that only about 25% of all the children who underwent adenoidec tomy were classified as having so-called ade noid facies Furthermore adenoid facies was judged to be present in about 4% of the controls The number of children with so-called adenoid facies would probably be somewhat higher in an unselected population than in the present control group since a number of adenoidectomy cases would be included in an unselected series This means that in a screen ing based on facial type, many cases that call for adenoidectomy would be missed at th same time as some of the cases selected would not be in need of adenoidectomy

In the comparisons with respect to variables for the facial skeleton, the children who under went adenoidectomy for obstructed nose breathing differed significantly from the controls. The facial characteristics that distinguished the group of children who underwent adenoidectomy on account of obstructed nose breathing were as follows. large face height, large angles between the mandibular line and the nasal and nasion sella lines, a tendency to small values for the angles s–n–ss and s–n–sm small sagittal depth of nasopharynx, small index values for face width/face height, cranial base depth/face height and face depth/face height, as well as large height of upper and lower lips The skeleton variable of greatest importance for mouth breathing appears to be size of nasopharynx. As already pointed out, the combination of large adenoids and small nasopharynx is commonly accompanied by mouth breathing Other skeleton variables appear to be of subordinate interest in this respect The skeletal type that was found to characterize mouth breathing in this study is distinguished in the first place by skeletal charac teristics that are correlated to size of nasopharynx and, in the second place by skeletal characteristics that may give a predisposition for the development of adenoids

It is also noteworthy that the children who underwent adenoidectomy solely on account of recurrent otitis media did not display the distinguishing characteristics that marked the facial skeleton of those with nasal obstruction on account of adenoids. In this respect, the former group did not differ significantly from the control children

From this it can be concluded that adenoids

occur in children of various facial types. Obstructed nose breathing on account of adenoids appears to be most common among children with a leptoprosopic type of face and a small nasopharynx.

Is tongue position affected by adenoids?

The question whether children with large adenoids have a different tongue position from those whose airways are free must be related to the question of whether they breath through the mouth. It has been maintained that the tongue is held low in mouth breathing (Subtelny 1954 Holik, 1957 Ricketts, 1958 *a*) and it appears natural that this should be so

A clear relationship between size of adenoids and tongue position was found for the children in the present study The relationship indicates that children with large adenoids hold the tongue low The same children also displayed a positive relationship between mouth breathing and a low tongue position.

Is the dentition affected by adenoids?

Whether and, if so, how adenoids are related to a particular type of dentition are questions that have been discussed in the literature ever since Tomes (1872) reported that children who are mouth breathers on account of large adenoids usually display contracted, V-shaped dental arches. It is not, however the presence of adenoids which is held responsible but the resultant development of mouth breathing. Special types of occlusion combined with adenoids and mouth breathing have been described for instance, by Bloch (1903), Michel (1908) Körbitz (1910), Izard (1925) Kantorowicz (1916) Wustrow (1917), Nervert (1939), Cooke (1940) McCoy (1941), Massler Poncher & Schour (1945) Subtelny (1954), Negus (1955) Duyzing (1963), Joshi (1964) and Ricketts (1968). The type usually described as a consequence of prolonged mouth breathing is a narrow V-shaped upper jaw with a high palatal vault, proclined upper incisors and a postnormal relation between the jaws. In the literature (e.g. Lischer 1912, Strang, 1933 Bowen & Balyeat, 1934 Neivert, 1939 McCoy 1941 Ballenger & Ballenger 1943 Subtelny 1954 Moyers, 1963 Hovell, 1966) proclination of the upper incisors in mouth breathers is usually attributed to reduced pressure from a short upper lip and a proclining force from the lower lip against the palatinal surfaces of the upper incisors.

The opposite opinion—that the type of dentition is not affected by the presence of adenoids combined with mouth breathing—has been maintained, for instance, by Kingsley (1888), McKenzie (1909) Whitaker (1911) Wallace (1927) Brash (1929), Howard (1932) Sillman (1942), Hartsook (1946), Huber & Reynolds (1946), Ballard & Gwynne Evans (1958), Leech (1958) Linder Aronson & Bäckström (1960) and Backlund (1963)

In the present study relationships were found between adenoids on the one hand and, on the other a narrow upper arch, crossbite or a tendency to crossbite, retroclined upper and lower incisors, a short lower arch and large angles between the occlusal line and the mandibular and nasion-sella lines. This type of dentition was also displayed by the mouth-breathing children. Thus the differences between the type of dentition usually attributed to mouth breathers and the results of this study chiefly refer to the inclination of the upper and lower incisors, the height of the palatal vault and the sagittal relationship between the upper and lower arches. It was furthermore found in the present study that a long upper lip was more common among the mouth breathers than among the nose breathers.

The retroclination of the upper incisors in the present mouth breathers can therefore be interpreted as a consequence of an influence of muscles of the upper lip when the mouth is held open. It is conceivable that this involves increased tension in the upper part of the orbicularis oris muscle, resulting in posterior pressure against the incisors because the tendon plates attaching this muscle at the angles of the mouth are held back in turn by the buccinator and triangularis muscles (Petrén 1948) The retroclination of

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In the present study photographs of the children were judged independently by two observers and it was found that only about 25 % of all the children who underwent adenoidectomy were classified as having so-called adenoid facies Furthermore adenoid facies was judged to be present in about 4 % of the controls. The number of children with so-called adenoid facies would probably be somewhat higher in an unselected population than in the present control group since a number of adenoidectomy cases would be included in an unselected series. This means that in a screening based on facial type, many cases that call for adenoidectomy would be missed at the same time as some of the cases selected would not be in need of adenoidectomy

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It is also noteworthy that the children who underwent adenoidectomy solely on account of recurrent otitis media did not display the distinguishing characteristics that marked the facial skeleton of those with nasal obstruction on account of adenoids. In this respect the former group did not differ significantly from the control children.

From this it can be concluded that adenoids

during an intermediary The hypothesis reproduced in the heading to this section recognizes that the presence of adenoids is associated with mouth breathing and that a low tongue position is more common in children who are mouth breathers than in those who are not.

The analyses in this study have shown that the variable for mouth breathing serves as a link in the relationship between adenoid variables and the dentition variables for the angle between the upper incisors and the nasion-sella line and the angle between the lower incisors and the mandibular line. The variable for tongue position, on the other hand, lacked importance as a link in this relationship This may possibly support the opinion that mouth breathing affects these angles via lip pressure, when the mouth is held open, rather than via a low tongue position.

Concerning the width of the upper arch between first molars, a significant relationship was only found with size of adenoids In this connection it should be remembered that nasal obstruction from adenoids is more pronounced in children with a special facial type, e.g. a long and/or narrow face and a small nasopharynx. It should be emphasized, however that conclusions based on these analyses do not rule out the possibility of other mechanisms in the relationships demonstrated between adenoids combined with mouth breathing and various characteristics of the dentition.

In order to throw further light on the question whether the relationship between adenoids and dentition variables can be explained by adenoids causing mouth breathing and this in turn affecting tongue position and thereby the dentition, studies are required, for instance concerning the development of the dentition after adenoidectomy in mouth breathers, since this operation can be expected to affect size of adenoids, mode of breathing and tongue position.

Since the combination of adenoids and mouth breathing appears to affect the dentition to some extent, assessments of the indications for adenoidectomy should include an orthodontic evaluation.

upper incisors in mouth breathers can moreover be regarded as a parallel phenomenon to the facial type of these children Thus it has been reported by Leech (1958) that Angle Cl. II 2 is more common than Cl. II 1 in individuals with large adenoids

The retroclination of the lower incisors in the present mouth breathers is also interpreted as a result of increased tension in the orbicularis oris muscle when the mouth is held open, the mechanism corresponding to that outlined above for the upper incisors with the zygomaticus major and caninus muscles acting in stead of triangularis A low tongue position in mouth breathing (Subtelny 1954 Holik 1957 Ricketts 1958 *a*) with the tongue possibly held withdrawn as well may have been a contributory cause (Hovell 1962) This retroclination probably also represents a parallel phenomenon to the facial type of these mouth breathers In this context it should be noted that, in relation to the nasal and nasion-sella lines, the mandibular line lay approximately 5 more backwards–upwards in the mouth breathers compared with the controls which should give the former a smaller angle between the lower incisors and the mandibular line

The relationship between a high palatal vault and adenoids combined with mouth breathing that has been described for instance, by Körbitz (1910) Kantorovicz (1916) Wustrow (1917) Izard (1925) Cooke (1940) and Massler Poncher & Schour (1945) could not be demonstrated in the present children

In the analysis in this study of the relationship b tween an index for height of palatal vault and width of upper arch between first molars on the one hand and, on the other adenoids and mouth breathing it was found that a narrow upper arch and/or a high palatal vault occurs more frequently in mouth breathers than in nose breathers. Mouth breathing in the former individuals is to be regarded as a consequence rather than a cause of a narrow upper arch and/or a high palatal vault In this context, the relationship between arch width and mouth breathing is considered to be stronger than that between height of palatal vault and mouth breathing. A similar opinion has been expressed by Subtelny (1954) namely that the impression of a high palatal vault in mouth breathers can be explained as an optical illusion due to a narrow upper arch

The relationship reported between adenoids combined with mouth breathing and a postnormal occlusion, e.g by Angle (1907) McCoy (1941) Hemley (1944) Massler Poncher & Schour (1945) Graber (1961) and Joshi (1964) could not be verified in the present study

In keeping with previous reports that children with adenoids combined with mouth breathing often have a narrow upper arch (e g. Tomes, 1872 Cooke, 1940 McCoy 1941 Massler Poncher & Schour 1945 Subtelny 1954 Negus, 1955 Duyzing, 1963 Moyers, 1963 Ricketts, 1968) the present children who underwent adenoidectomy for obstructed nose breathing were found to have a narrow upper arch more frequently than the nose breathers A small upper arch in these adenoidectomy children could be explained as a parallel phenomenon to their long, narrow type of face with a small nasopharynx and narrow nose. This, however does not rule out the possibility of a certain causal relationship between upper arch width and adenoids, with mouth breathing and a low tongue position as a result This question can best be elucidated by follow up studies after adenoidectomy

The relationships obtained in this study between adenoid and dentition variables confirm the assumption that a relationship exists between the presence of adenoids and special characteristics of the dentition

Can the relationship between the presence of adenoids and dentition variables be attributed to adenoids resulting in mouth breathing which in turn affects tongue position and thereby the dentition?

The relationships described between the presence of adenoids and dentition are difficult to explain in direct causal terms without intro-

ducing an intermediary The hypothesis reproduced in the heading to this section recognizes that the presence of adenoids is associated with mouth breathing and that a low tongue position is more common in children who are mouth breathers than in those who are not.

The analyses in this study have shown that the variable for mouth breathing serves as a link in the relationship between adenoid variables and the dentition variables for the angle between the upper incisors and the nasion-sella line and the angle between the lower incisors and the mandibular line. The variable for tongue position, on the other hand lacked importance as a link in this relationship This may possibly support the opinion that mouth breathing affects these angles via lip pressure, when the mouth is held open, rather than via a low tongue position.

Concerning the width of the upper arch between first molars, a significant relationship was only found with size of adenoids. In this connection it should be remembered that nasal obstruction from adenoids is more pronounced in children with a special facial type, e.g. a long and/or narrow face and a small nasopharynx. It should be emphasized, however that conclusions based on these analyses do not rule out the possibility of other mechanisms in the relationships demonstrated between adenoids combined with mouth breathing and various characteristics of the dentition

In order to throw further light on the question whether the relationship between adenoids and dentition variables can be explained by adenoids causing mouth breathing and this in turn affecting tongue position and thereby the dentition, studies are required, for instance concerning the development of the dentition after adenoidectomy in mouth breathers, since this operation can be expected to affect size of adenoids mode of breathing and tongue position.

Since the combination of adenoids and mouth breathing appears to affect the dentition to some extent, assessments of the indications for adenoidectomy should include an orthodontic evaluation.

General summary

Chapter 1 reviews the literature concerning adenoids in relation to mode of breathing as well as to special facial types and dentition characteristics

Chapter 2 presents the purpose of the present study namely·

(*a*) to study which relationships exist between adenoids and variables representing mode of breathing, airflow and type of dentition

(*b*) to study how mode of breathing airflow and type of dentition are related to certain variables for the facial skeleton,

(*c*) to try to establish whether there is a relationship between adenoids and the occurrence of so-called adenoid facies, and

(*d*) to try to establish whether a modified tongue position in the presence of adenoids represents an etiological factor for malocclusion

Chapter 3 describes the material and methods

The present investigation was conducted on 162 children from the county of Örebro in Central Sweden born in the years 1955–61

The patients (81) comprise children selected for adenoidectomy by otologists The controls (81) were chosen on the basis of the adenoidectomy children's age, sex and number using the National Register

The same studies were made on adenoidectomy children and controls. The material is separated into 5 different groups The controls are divided between groups 1–3 depending on the size of adenoids as studied on lateral cephalometric radiographs group 1 no adenoids group 2 small or moderate adenoids group 3 large adenoids

Group 4 comprises the children who underwent adenoidectomy on account of recurrent otitis media only and group 5 those who underwent the operation for obstructed nose breathing, with or without otitis media.

All the subjects have been studied with respect to 173 variables, grouped as anamnesis adenoid, dentition, airflow skeleton-lip and tongue variables. Data on each subject include direct facial measurements a photograph of the face, measurements on lateral and frontal radiographs, measurements on casts and recordings of nasal airflow at differential pressures of 10 15 and 20 mm H_2O

The method for measuring nasal airflow consists of simultaneous recordings of the rate of airflow and the pressure gradient between the nasopharynx and the nostrils The recordings were made before and 15 min after the administration of nose drops on two occasions one month apart Adenoidectomy was performed on all the subjects in groups 4 and 5 between these two occasions

Chapter 4 presents the errors of method for all the variables

Charpter 5 describes the statistical methods used for the analysis of relationships, namely simple correlation analysis and multiple regression analysis.

All calculations in this study have been performed on the UDAC (Uppsala computer CDC 3600)

Chapter 6 describes the results of comparisons of means between the control and adenoidectomy groups as well as the results of the simple correlation analyses For the children in this study these results show that

the division of the material into groups 1–5 is fully justified In this context it is particularly noteworthy that the children who underwent adenoidectomy for obstructed nose breath-

ing (group 5) differ significantly in several respects not only from the controls in groups 1 and 2 but also from the children who under went adenoidectomy on account of otitis media (group 4)

the controls include 11 children (group 3) with no clinical discomfort in spite of having large adenoids

adenoids lead to mouth breathing;

size of adenoids decreases with increasing age

good agreement was found between clinical assessments of size of adenoids and measure ments on radiographs,

the children who underwent adenoidectomy for obstructed nose breathing had larger ade noids in relation to the nasopharynx than those who underwent the operation on account of recurrent otitis media

nasal airflow measured at a differential pres sure of 10 mm H_2O is lower for large than for small adenoids and increases after adenoidec tomy

there is a relationship between the presence of adenoids and particular characteristics of the dentition. Compared with children who have no adenoids, those with adenoids and obstructed nose breathing more frequently pre sent a narrow upper arch, crossbite or a ten dency to crossbite retroclination of upper and lower incisors in relation to the base lines, a short lower arch and large angles between the occlusal line and the mandibular and na sion-sella lines

adenoids with obstructed nose breathing as a result is commonly associated with a particu lar type of facial skeleton. Compared with children who have no adenoids, those who underwent adenoidectomy for obstructed nose breathing more commonly present a large face height, large height of upper and lower lip, a tendency to small values for the angles s–n–ss and s–n–sm, large angles between the mandi bular line and the nasion-sella and nasal lines and small index values for face width/face height, cranial base depth/face height and face

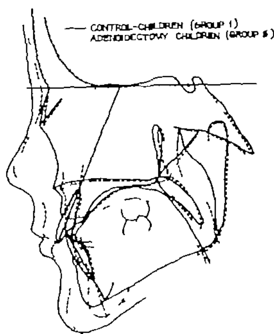


Fig 39 Tracings of lateral cephalometric radiographs showing significant differences between the children who underwent adenoidectomy for obstructed nose breathing (group 5) and the controls (group 1) with respect to variables representing adenoids, the dentition, the skele ton, lips and position of the tongue

children with adenoids and obstructed nose breathing more often hold the tongue low than those without adenoids.

A composite picture of the differences be tween groups 1 and 5 is given in Fig. 39 *Chapter 7* describes the results of the mul tiple regression analyses. For the children in this study these results show that:

mouth breathing can largely be explained as a consequence of size of adenoids and size of the bony nasopharynx

nasal airflow measured at a differential pres sure of 10 mm H_2O is determined in the first place by size of adenoids and sagittal depth of the bony nasopharynx. Furthermore, the size of the nasopharynx is of little importance for airflow when the adenoids are very large and block the passage of air The size of the nasopharynx is also of little importance for airflow in the absence of adenoids, since the

General summary

Chapter 1 reviews the literature concerning adenoids in relation to mode of breathing as well as to special facial types and dentition characteristics

Chapter 2 presents the purpose of the present study namely·

(*a*) to study which relationships exist between adenoids and variables representing mode of breathing, airflow and type of dentition

(*b*) to study how mode of breathing, airflow and type of dentition are related to certain variables for the facial skeleton

(*c*) to try to establish whether there is a relationship between adenoids and the occurrence of so-called adenoid facies, and

(*d*) to try to establish whether a modified tongue position in the presence of adenoids represents an etiological factor for malocclusion.

Chapter 3 describes the material and methods

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The patients (81) comprise children selected for adenoidectomy by otologists The controls (81) were chosen on the basis of the adenoidectomy children's age sex and number using the National Register

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Acknowledgements

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Örebro, October 1969

Sten Linder Aronson

passage of air is then sufficient regardless of the size of the nasopharynx It is chiefly in children with small or moderate adenoids that the sagittal dimension of the nasopharynx is of essential importance for the magnitude of the nasal airflow

the upper incisors were retroclined in relation to the nasion-sella line in many of the children in adenoidectomy group 5 as well as in children with a large overbite, a small lower face height or a small value for the angle s–n–ss

the lower incisors were often retroclined in relation to the mandibular line in children who breath through the mouth, have a large angle between the mandibular and nasal lines or a small overjet

a narrow upper arch between first molars is often found in children with a small nasopharynx, short crowded upper jaw or a large angle between the nasal and mandibular lines

large overjet is often found in children with a large value for the angle ss–n–sm a long upper arch, a large sagittal dimension on the roof of the nasal cavity or a postnormal relation between the upper and lower first molars

a small overbite is often found in children with crossbite or a tendency to crossbite or a small index value for anterior upper and total face height

the size of the index for height of palatal vault and upper arch width betwen first molars is primarily dependent on the age of the child A narrow upper arch and/or a high palatal vault was frequently found in the children who were mouth breathers

a large angle between the mandibular and nasal lines is frequently found among children with large values for the angle ss–n–sm small values for the angle ss–n–ba, long upper and lower lips or a short anterior cranial base length

the relationship between size of adenoids and mouth breathing on the one hand and, on the other dentition variables such as the angle between the upper incisors and the nasion-sella line, the angle between the lower incisors and the mandibular line and the width of the upper arch between first molars, could not be explained by tongue position

Chapter 8 describes the number of observed and expected significant analyses at the 5%, 1% and 0 1% levels

Chapter 9 is concerned with the frequency of so-called adenoid facies. Assessments of this frequency from photographs show that it is significantly higher for the adenoidectomy children than for the controls. In the present study it was found that so-called adenoid facies was presented by approximately 25% of the children who underwent adenoidectomy on account of recurrent otitis media or obstructed nose breathing Adenoid facies was also noted in approximately 4% of the children in the control groups.

The results obtained in this study appear to support the present hypothesis that adenoids affect the mode of breathing, which then influences the individual's dentition.

This, of course, does not rule out the possibility that other more complex causal relationships are also involved The correlation between a narrow nasopharynx and mouth breathing indicates that a particular structure of the facial skeleton influences the development of mouth breathing It is also conceivable that the structure of the facial skeleton directly influences the development or the size of adenoids Any such structure that predisposes for adenoids may in itself involve associations to certain characteristics of the dentition that have been found to be connected with mouth breathing Further elucidation of various conceivable causal mechanisms calls for studies of the development of the dentition after adenoidectomy in mouth breathers As mentioned on p 16 such an investigation is being conducted and will be published separately

$$\frac{r}{\sqrt{1-r^2}}\sqrt{n-2}$$

which—if the true correlation was zero—was considered to be distributed like Student's t with n-2 degrees of freedom.

Significance levels

The term "significant" is used in accordance with the following convention. If an observed difference between two means is of such magnitude that the probability P of obtaining a difference at least as great as the observed value is greater than 0.05 (where the null-hypothesis is assumed to hold), then that observed difference is said to be non-significant.

If $0.01 < P < 0.05$, the difference is said to be almost significant and is marked

If $0.001 < P < 0.01$ the difference is said to be significant and is marked

If $P < 0.001$ the difference is said to be (highly) significant and is marked

Multiple regression analysis used in the present study

For a series of n children we wish to study the relation between a dependent variable, y called the regressand, and a set of explanatory variables, $x^{(1)}$ ... $x^{(k)}$ called regressors. The regressands are variables indicating mode of breathing, air flow and bite characteristics, etc. The k regressors $x^{(1)}$ $x^{(2)}$ ... $x^{(k)}$ may be age, sex, size of adenoids, etc.

In order to study the relation between the y and x variables, a type of equation must first be laid down. Individual numerical values must also be available for each variable. In the present work equations of the following form have been studied

$$y = b_0 + b_1 x^{(1)} + b_2 x^{(2)} + \ldots b_k x^{(k)}$$

where b_0, b b_2 ... b_k are the coefficients which are to be estimated. In estimating these coefficients the principle of least squares has been applied. This principle means that we seek values of coefficients which are constituted in such a way as to yield the smallest possible sum from the following expression

$$\Sigma(y - b_0 - b_1 x^{(1)} - b\ x^{(2)} \ldots b_k x^{(k)})^2$$

If this expression is treated in a purely mathematical fashion, as a maximum–minimum problem we obtain a general solution with the aid of the following $k+1$ linear equations in the $k+1$ unknown coefficients

$$\begin{cases} \Sigma y = b_0 n + b_1 \Sigma x^{(1)} + \ldots + b_k \Sigma x^{(k)} \\ \Sigma y x^{(1)} = b_0 \Sigma x^{(1)} + b_1 \Sigma x^{(1)} x^{(1)} + \ldots + b_k \Sigma x^{(k)} x^{(1)} \\ \Sigma y x^{(2)} = b_0 \Sigma x^{(2)} + b_1 \Sigma x^{(1)} x^{(2)} + \ldots + b_k \Sigma x^{(k)} x^{(2)} \\ \ldots \\ \Sigma y x^{(k)} = b_0 \Sigma x^{(k)} + b_1 \Sigma x^{(1)} x^{(k)} + \ldots + b_k \Sigma x^{(k)} x^{(k)} \end{cases}$$

Here Σy stands for the sum of all individual y values and $\Sigma y x^{(1)}$ the sum of all individual products of $y x^{(1)}$ etc.

The principle of least squares has been described in detail by Cramér (1945) and Hald (1948), who also explain the method of calculating S.E. for the coefficients.

Predicted value

The y value for an individual (i), predicted with the aid of the regression equation, is defined as

$$b + b_1 x^{(1)} + b_2 x_i^{(2)} + \ldots + b_k x_i^{(k)}$$

All statistical analyses were performed in collaboration with Associate Professor G. Eklund, Ph.D. at the Department of Statistics, University of Stockholm.

Appendix

STATISTICAL METHODS

Notation

Number of cases N or n the latter in the event of missing values.

Mean $M = \bar{X} = \frac{\sum X_i}{n}$ or $\frac{\sum X_i}{N}$

where X_i denotes the value for the ith case.

Standard deviation

$$S.D. = \sqrt{\frac{\sum(X_i - M)^2}{n-1}}$$

Standard error of the mean

$$S.E. = \frac{S.D.}{\sqrt{n}}$$

Standard error of the difference between two means, $\bar{x}$ and $\bar{y}$

$$S.E._{\bar{x}-\bar{y}} = \sqrt{S.E._{\bar{x}}^2 + S.E._{\bar{y}}^2}$$

Regression analysis

Correlation analysis The correlation coefficient, r of x and y is defined by the expression

$$r = \frac{\sum(x_i - \bar{x})(y_i - \bar{y})}{\sqrt{\sum(x_i - \bar{x})^2 \sum(y_i - \bar{y})^2}}$$

where $\bar{x}$ and $\bar{y}$ denote the means for the x and y series respectively

The partial correlation coefficient between x and y with z held constant.

$$r(xy.z) = \frac{r(xy) - r(xz)\, r(yz)}{\sqrt{(1 - r^2(xz))(1 - r^2(yz))}}$$

The residual value for an individual (i) is defined as the observed y value minus the predicted y value.

The residual variance is defined as

$$\frac{\sum \text{residuals}^2}{n-k-1} = \frac{\sum(y - b_0 - b_1x^{(1)} - b_2x_i^{(2)} \dots b_kx^{(k)})^2}{n-k-1}$$

where $b_0, b_1 \dots b_k$ denote the estimated coefficient values.

The standard deviation of the residuals (R.S.D.) is defined as the square root of the residual variance

The coefficient of determination, R^2 i.e. the square of the multiple correlation coefficient, is

$$R^2 = 1 - \frac{(n-k-1)\ \text{residual variance}}{\sum(y_i - \bar{y})^2}$$

The residual variance is that part of the variance which remains after the effect of the regressors (independent variables) is removed. It measures the variability due to unexplained causes and irregular measurement error

R^2 *serves as a measure of the part of the re*gressand's variance that is due to the regressors. If the regressors are direct or indirect causal factors of the regressand, the value of R^2 can be said to express their explanative value.

Significance tests

1 In testing the difference between two percentages the χ^2 test with one degree of freedom was used. Yates correction was applied

2. In testing differences between means, the following approximately t-distributed ratio was formed

$$t = \frac{\bar{x} - \bar{y}}{S.E.}$$

3 In testing whether the regression coefficients differed from 0 the method described by Cramér (1945) and Hald (1948) was used

A t value was produced from the expression $b_j/S.E._{b_j}$

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Defects of the auditory ossicles in ears with intact tympanic membrane

Clinical studies

BY

OLE ELBRØND

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DEFECTS OF THE AUDITORY OSSICLES IN EARS WITH INTACT TYMPANIC MEMBRANE

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ÅRHUS 1970

CONTENTS

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The development of surgery for otosclerosis has produced considerable knowledge of the pathology of the middle ear and, in the process, provided information on other conductive hearing defects which occur with an intact membrane, but which are not of otosclerotic nature. Sooy (1960) reported that, in more than 1100 tympanotomies performed in cases of suspected otosclerosis, 4.2 per cent of the hearing defects were shown to have non-otosclerotic causes. Among these causes it was found that defects in the auditory ossicles (i. e. loss of continuity for any reason) formed an important group.

An exposition of the aetiological factors involved in defects of the auditory ossicles occurring while the tympanic membrane remains intact will be found in the following:

I. Traumatic Fractures and Dislocations of the Auditory Ossicles

A. Fractures and luxations of the auditory ossicles due to cranial traumata.

Such conductive interruptions have frequently been described in the literature in recent years. This is most probably due to three factors:

1 An increasing number of cranial traumata resulting from the explosive development of modern traffic and industry

– An increased survival rate among this type of patients due to more effective therapy during the acute phase permits diagnosis, during a following quiet phase, of traumatically caused hearing defects, and likewise permits surgical intervention in cases of defects in the transmission system of the middle ear

3 The intensive development of otological surgery which has led to an increased probability of succes with reconstructive treatment of the transmission mechanism of the middle ear

Most of these cases will involve patients with longitudinal fractures of the petrous part, as transverse fractures through the petrous part will, as a rule, involve the labyrinth, and thus result in loss of the labyrinthial function. In cases of longitudinal fractures, the labyrinthial function will most often be retained, even though a high-frequency perceptive hearing loss of greater or lesser magnitude will be observed, occasionally with a simultaneous conductive hearing loss (Escher 1964)

A typical longitudinal fracture of the petrous part will often result in damage to the middle ear at one point or another As a rule, the fracture line runs from the squamous portion of the temporal bone through the external meatus, tympanic groove, tegmen tympani, passes by the labyrinth and terminates at one of the openings in the base of the skull. The preferred course of the fracture follows the roof, the transition between the roof and the posterior wall, and the posterior wall (Kley 1966) The courses of the fractures, together with displacement of bone fragments and the magnitude of the forces at the instant of the trauma, determine the type and extent of the injury to the auditory ossicles.

Most frequently the fracture follows the upper posterior edge of margo tympanicus, and thus passes very near the incus. As the incus is, in addition, the least stably fixed of the three bones (the other two are stabilized by the tensor tympani muscle and the stapedius muscle in addition to ligaments and, in case of the malleus, by the tympanic membrane as well)

INTRODUCTION

The introduction of tympanoplastic surgery by Wullstein and Zöllner has caused considerable activity toward improvement of the results of such treatment.

These efforts have primarily been concentrated on the development of the most suitable myringoplastic procedures. However during the past few years, there has been a growing interest in reconstructive surgery on the auditory ossicles.

The object of the present work is—partly on the basis of studies of the literature, and partly on the basis of original clinical and previously published experimental studies—to illustrate the aetiological, diagnostic, and reconstructive problems arising in connection with defects of the auditory ossicles when the tympanic membrane is intact, so that it may become possible to improve the results of reconstructive surgery on the ossicular chain.

an explosion, boxing the ears, or the like, may also lead to dislocation of the incus (Escher 1964).

II. Defects in the Auditory Ossicles Resulting from Disease

Necrosis of the lenticular process and the distal end of the long process of the incus are occasionally revealed by tympanotomy in patients who are able to recall the incidence of otitis media at an earlier date. Numerous authors have reported such cases (Hamberger and Lidén, 1958 Gilmel, 1958 Hough, 1959 Sooy 1960 Andersen et al., 1962) The bony structure will often be found to have been replaced by a fibrous cord which permits the transmission of sound only to a very limited degree. On occasion it will be seen that only the distal end of the long process of the incus has been replaced by fibrous tissue, while the lenticular process remains intact and connected to the head of the stapes by the joint capsule. The long process of the incus thus seems to be more vulnerable to the influences of inflammation than do the remaining parts of the ossicular system, but on rare occasions coincident necrosis of the stapes crura is also revealed.

Ostitis of the ossicles, and the pressure of granulation tissue during the suppurative stage, can result in defects in the long process of the incus and the stapes crura.

It seems likely that a capillary insufficiency may well be a contributory cause of such post inflammatory necroses. A significant portion of the blood supply to the distal parts of the long process and the lenticular process is provided by passages in the mucous membrane covering the bone (Alberti, 1963) If this capillary net work is damaged as the result of inflammation in the middle ear conditions suitable for osteonecrosis might well be present. It is well known that necrosis of the long process of the incus and the lenticular process can be seen after stapes operations (Alberti and Dawes, 1961 Smith, 1966 Webb et al., 1966) This is true for both stapes mobilization and stapedectomy The cause of the necrosis in these cases is given as the traumatization of the mucous membrane—including the capillaries—both locally at the lenticular process and the long process of the incus as well as the stapes tendon.

III. Auditory Ossicular Defects Resulting from a Cholesteatoma

Cholesteatoma is not infrequently found where there is no anamnesis of otitis media and the tympanic membrane is intact (Riedl, 1957 Everberg, 1965)

A cholesteatoma obviously may injure the ossicles or disrupt their functional continuity

IV Radiation-Induced Defects of the Auditory Ossicles

Necrosis of the long process of the incus may be found after radiation treatment of malignant tumours in the region of the middle ear Gyorkey and Pollock (1960) have described a case of necrosis of the long process after radiation therapy for an ependymo-blastoma in the bottom of the fourth ventricle. It is suggested that a reduced or interrupted capillary supply to the bone, caused by the radiation, may have contributed to the necrosis. Radiation treatment of malignant tumours in the rhino-pharynx may also result in necrosis of the long process (Andersen et al., 1962).

V Congenital Defects of the Auditory Ossicles

Any disruption of the development of the first two branchial arches can result not only in facial deformities such as Franceschetti's Syndrome, but in deformities of the ear of greater or lesser severity as well (Altmann, 1955 Edwards, 1964 Mündnich, 1965) The interesting point in this connection is that there are cases where the deformities are primarily localized in the ossicles, while the inner ear develops normally De Witt (1958) has given this condition the designation *atresia auris minima*.

According to Ombrédanne (1959) these cases can be separated into three groups.

the incus will be the bone most likely to suffer dislocation Therefore, it should not be surprising that incus luxations have been described by many authors (Thorburn, 1957 Gisselson 1958 Bauer 1958 Flisberg and Floberg, 1960 Andersen et al 1962 Ballantyne 1962 Anklesaria 1963 Hammond, 1964 Escher 1964 Does and Bottema 1965) A luxation of the incus can vary from a very slight displacement of the lenticular process of the head of the stapes, with only partial laceration of the joint capsule to complete loosening of the incus and its displacement to for example the external meatus, the mouth of the Eustachian tube or the antrum It is also possible that a dislocation on the incus may occur in connection with a fracture of one or both of the stapes crura, as there is a significant variation in the massiveness and thus, also in the strength of the crura.

If the fracture should go through the tympanic groove in close proximity to the head of the malleus, there may occur a luxation of the malleus, either alone or with the incus (Hammond, 1964 Kley 1966)

In the case of a horizontal fracture through the mastoid process, involving the posterior edge of the margo tympanicus, Kley (1966) reports that a fracture of the handle of the malleus or the long process of the incus is possible

Isolated stapes fractures have been described by several authors (Williams, 1958 Robinson, 1961 Rietjens 1963 Sadé 1964 Andersen and Elbrønd, 1968) It may be postulated that such fractures have occured as the result of a temporary dislocation or subluxation of the incus (Kley 1966) A powerful coincident contraction of the stapedius muscle (caused by the trauma) can also be suggested as contributory to the dislocation (Hough, 1959)

Finally it should be mentioned that longitudinal fractures in the petrous part are often accompanied by bleeding from the ear and, not infrequently by leakage of cerebro-spinal fluid as well I severe cases, brain tissue may also be found in the tympanic cavity and in the Eustachian tube. A facial paralysis will be found in approximately 15 per cent of these cases.

B *Operatively-caused Dislocations of the Incus*

A mastoidectomy or antrotomi is not infrequently complicated by a dislocation of the incus when the cells around the entrance to the antrum must be drained (Plester 1957 Schuknecht and Trupiano 1957 Riskær 1960 Andersen et al 1962 Escher 1964) This type of luxation is naturally more prone to occur when these cells are emptied without the use of a surgical microscope This luxation consists in the loosening of the ligaments which connect the short process of the incus to the wall of the fossa incudis.

It is well known that mastoidectomy was previously performed very frequently but the use of antibiotics in the treatment of otitis media has resulted in a significant decrease in the number of these operations. A luxation due to surgical treatment will thus occur very seldom.

C. *Transmeatal Lesions of the Ossicular System*

Puncture injuries, caused by a knitting-needle straw twig etc. inserted through the external meatus, occasionally result in injuries to the auditory ossicles. Escher (1964) describes a case of stapes fracture after a knitting-needle puncture Incautious therapeutic manipulations can also lead to disruption of the continuity of the ossicles. Escher (1964) mentions a luxation of the malleus caused by the end of an ear syringe Unfortunate cases of simple tympanic puncture resulting in a luxation of the incudo-stapedial articulation or fracture of the stapes, are also recorded. In all of the above-mentioned cases, a lesion in the tympanic membrane will naturally occur at the time of the injury but as a rule this will heal and not infrequently this healing will proceed without leaving a trace of the puncture. Shock wave traumata through the meatus, caused by

DIAGNOSIS

Defects in the auditory ossicles, and a number of other diseases of the middle ear where the tympanic membrane remains intact and the Eustachian tube is functional (especially fixation of the ossicles due to infectious, traumatic, or congenital causes) result in a conductive loss of hearing in common with otosclerosis. These *conditions are therefore* sometimes given the designation "pseudo-otosclerosis (Goodhill, 1960) and they can provide difficulties in the differential diagnosis.

The following points will be of diagnostic significance:

1 Anamnesis. The patient's history may often include information which can lead to a diagnosis.

Information about any familiar tendency toward a loss of hearing will be significant. Such a tendency will support a diagnosis of otosclerosis. The point in time at which the hearing loss apparently began may also aid the diagnosis, as otosclerosis begins, as a rule, during the second decade of life. Information about a lack of tinnitus, and a purely one-sided loss of hearing, can also provide grounds to suspect an ossicular defect.

A conductive loss of hearing of permanent and stable character following upon a cranial trauma, will naturally lead to a suspicion of ossicular luxation or fracture. However the ossicles may be prevented from functioning properly due to fixation by a bone fragment (e. g. a fracture through the area of the tegmen tympani may have this type of effect), a traumatic stenosis of the Eustachian tube or adhesions in the tympanic cavity following a hematotympanum will likewise lead to a conductive loss of hearing.

A permanent loss of hearing in connection with a mastoidectomy or a lesion through the external meatus will indicate as a rule, a luxation of the incus. A conductive loss of hearing after otitis media, with the tympanic membrane remaining intact, will often be caused by a fibrous degeneration of the long process of the incus and/or the stapes crura, but it may just as well be due to an infection being followed by a fixation of the ossicles (adhesions, tympano-sclerosis, etc.)

Now and then, one may receive patients who are unable to recall any details of the incidence of otitis media, while their tympanic membranes bear the imprint of the infection (calcium deposits, fibrosis, atrophic or retracted zones). It must be natural to assume that these persons have suffered from an otitis media during their early childhood, and that the loss of hearing is therefore probably due to a defect in the ossicles, perhaps an infectiously-caused fixation of one or more of the bones.

Patients having a conductive loss of hearing which already has been observed during their childhood should be suspected of having an ossicular deformity especially where there is a unilateral loss of hearing and/or the patient is found to harbour other anomalies.

At times, patients are found to have defects in the auditory ossicles, while the anamnesis does not indicate any of the above-mentioned causes, and where the hearing loss has developed gradually and the tympanic membrane is quite normal. (As previously mentioned, Escher and Neiger (1963) have called this condition aseptic necrosis of the ossicles)

2. Otoscopic Examination. In the case of ossicular lesions of traumatic nature, the tym-

1 Cases where the deformity is discovered accidentally during an explorative tympanotomy performed because of a suspected otosclerosis.

2 Cases where superficial deformities such as a slight facial asymmetry unequeal functioning of the lower branch of the facial nerve preauricular fistula accessory auricular appendages asymmetry of the external ear or a slight atrophy of the mandibula permit the preoperative assumption that the conductive loss of hearing is caused by a deformity in the ossicles. A slight narrowing of the meatus perhaps with exostoses, or a thickened tympanic membrane with a widened handle of the malleus, should also be mentioned in relation to the above

3 Cases, especially among children where there may be a pre-operative suspicion of an ossicular deformity based upon the indication of a severe unilateral non progressive conductive loss of hearing

One two, or all three of the auditory ossicles may be deformed (Hough 1963)

Malleus The handle of the malleus may be lacking, and an insufficient development of the articulation between the incus and malleus has likewise been observed. The head of the malleus may be larger than normal and thus come in intimate contact with the tegmen tympani where it may become ossified to the roof of the epitympanic recess (Altmann, 1955 Mündnich, 1965)

Incus. There may be hypoplasia (De Witt 1958) or the incus may be totally lacking (Hajek 1961) The lenticular process may be completely absent, or replaced by a fibrous band (Henner 1960) The same may be true for a greater or lesser portion of the long process of the incus (Hough, 1958 Tolan and Wilson 1958 Hajek, 1961) It must be emphasized however that it may be difficult to determine whether a defect in the long process is post infectious or congenital.

Stapes. Of the three ossicles, the stapes is reported to be most subject to congenital deformities This will most often consist in a fixation of the stapes footplate (House et al., 1958) due to insufficient development of the annular ligament, but a complete lack of the oval window may be observed (Gundersen, 1967) Insufficient development of one (Hough, 1958) or both stapes crura (Henner 1960) may also be observed.

Occasionally a partial or total fusion of all three of the ossicles is described (Hough, 1958 Hajek 1961) as is the fusion of the malleus to the incus alone (Henner 1960)

Together with the ossicle deformities, one may find an abnormal routing of the facial nerve large dehiscences in the bony facial canal (Hough 1963 Scheer 1967) or the development of the pyramidal eminence the stapedius tendon and the round window may be lacking.

VI Auditory Ossicle Defects of Unknown Aetiology

Now and then an explorative tympanotomy will disclose a fibrous degeneration of the long process of the incus and/or the stapes crura where neither the anamnesis nor the objective indications provide a basis for suspecting one of the above-mentioned conditions as being causative Escher and Neiger (1963) have given such conditions the designation "aspectic bone necrosis"

A necessary condition is that the malleus is mobile. A defect in the ossicular system may permit excessive mobility of the malleus. This allows a stronger registration of the tensor reflex than is normal (which may, for example, be observed on the screen of an oscilloscope) as reported by Rietjens (1953). It must be assumed that a normal reflex is demonstrable in the opposite ear. Quantitative impedance measurements will probably provide valuable information about the condition of the ossicular system, especially relating to the differential diagnosis between fixations and defects.

5. An Acoustic Probe. This method (Zöllner 1951, Thullen, 1955) will probably be able to provide information permitting differentiation between defects and fixations in the ossicular system. The author has no experience with this method of examination.

6. Radiological Examination. Of the conventional X-ray projections, two have been shown to be significantly more *effective* in providing information about the state of the ossicles: The trans-orbital and the Chausse III. However, these projections can only provide information about the worst deformities, or about luxations which result in considerable separations between the ossicles (Andersen *et al.* 1962). Of 31 patients, all having defective ossicular systems, ten displayed pathological conditions in X-ray examinations using the above-mentioned projections.

Tomographical X-ray examinations can provide additional information about the condition of the ossicles (Mündnich and Frey, 1959, Langfeldt, 1963, Brünner, 1964, Valvassori, 1967). Using this technique Andersen et al., (1962) found pathological changes in the ossicular system in 16 of 21 patients, but only 11 of these radiological examinations were fully confirmed during the subsequent operations. In all of these cases, deformities or luxations of the incus or the malleus were disclosed. On the other hand, tomographical examination was revealed to be less valuable in cases of slight dislocations or defects localized in the incudostapedial articulation. But, as it will be shown in the Clinical Report II (see below), the tomographic X-ray examination has provided increasingly accurate information on the condition of the ossicles.

7. Tympanotomia Explorativa. As it may be seen from the material noted above, it *can be difficult* to provide pre-operative verification of a diagnosis of a defective ossicular system, even though this condition will often be suspected.

In numerous cases, a final diagnosis can only be reached during the explorative tympanotomy.

panic membrane will often be more or less cicatricial, especially the upper posterior sector of the drum Now and then it may be possible—especially with the aid of an operating microscope—to see through an atrophically translucent tympanic membrane and discern a luxation of the incudostapedial joint (Escher 1964)

Changes in the nature of the tympanic membrane in form of thickening, calcium deposits atrophic or retracted zones will often be seen when defects in the ossicles have developed after the ravages of otitis media

It should be noted that an examination of the mobility of the malleus and the tympanic membrane, using Siegle s speculum may provide information concerning the condition of the ossicles

3 Audiometric Examination The configuration of the typical otosclerosis audiogram is well known indicating a greater conductive loss for the low frequencies than for the high frequencies. In addition there is a drop in the bone-conduction curve at a maximum of about 2000 Hz (Carhart s Notch) The severity of the otosclerosis, and the extent to which the cochleae have been modified by it, will have a very considerable effect upon the configuration of the tone audiogram

In the case of a total disruption of the ossicular system with an intact tympanic membrane, the conductive loss of hearing could theoretically amount to approximately 60 dB (Wullstein 1960) throughout the entire frequency range. A hearing loss of this order is also seen now and then, no matter what the aetiology of the defective ossicles may be It must be emphasized however that the conductive hearing loss following these middle ear diseases can vary greatly as reported by Does and Bottema (1965) They found that a less severe hearing loss than might be expected could be caused by an adhesion formed between the stapes and the long process of the incus, the handle of the malleus, and the tympanic membrane Furthermore, they found several cases among their series of traumatically-caused ossicular defects where a perceptive high frequency hearing loss, or "dip" was displayed at C

Bauer (1964) provides the following audiometric characteristics for defects in the auditory ossicle system with an intact tympanic membrane

1 A conductive hearing loss of approximately 50 dB in the speech-frequency range,

2. The bone-conduction and the air-conduction curves for the greater part, follow parallel paths throughout the entire frequency range,

3 Carhart s Notch is not found in the bone conduction curve

4 Impedance Tests. Testing for changes in the impedance of the tympanic membrane—using an acoustic bridge (Metz, 1946) an electro-acoustic apparatus (Terkildsen and Scott Nielsen, 1960) or devices making use of the cross-coupling principle (Neergaard et al 1965)—can occasionally provide valuable information about the state of the ossicles.

A stapedius reflex caused by an acoustic stimulus (Jepsen 1955) or a cutaneous reflex stimulated by the direction of a stream of air upon the outer ear (Djupesland 1961) can be registered by the change occuring in the impedance of the tympanic membrane, but one of the conditions for this change is a functional, mobile ossicular system A defective or fixed ossicular system as a rule, will hinder or prevent the transmission of the contraction of the stapedius muscle along the ossicles, thereby changing the impedance of the tympanic membrane However it will be possible to record a stapedius reflex if the interruption in the ossicular system lies medially to the insertion of the stapedius tendon. In general this will indicate a fracture of the stapes crura (Rietjens, 1963 Andersen and Elbrønd 1968) A contraction of the tensor tympani muscle can be stimulated by directing a stream of air against the eyes. This reflex can also be registered through a change in the impedance of the tympanic membrane (Klockhoff 1961)

A necessary condition is that the malleus is mobile. A defect in the ossicular system may permit excessive mobility of the malleus. This allows a stronger registration of the tensor reflex than is normal (which may, for example, be observed on the screen of an oscilloscope) as reported by Rietjens (1953). It must be assumed that a normal reflex is demonstrable in the opposite ear. Quantitative impedance measurements will probably provide valuable information about the condition of the ossicular system, especially relating to the differential diagnosis between fixations and defects.

5. An Acoustic Probe. This method (Zöllner 1951, Thullen, 1955) will probably be able to provide information permitting differentiation between defects and fixations in the ossicular system. The author has no experience with this method of examination.

6. Radiological Examination. Of the conventional X-ray projections, two have been shown to be significantly more effective in providing information about the state of the ossicles. The trans-orbital and the Chausse III. However, these projections can only provide information about the worst deformities, or about luxations which result in considerable separations between the ossicles (Andersen et al., 1962). Of 31 patients, all having defective ossicular systems, ten displayed pathological conditions in X-ray examinations using the above-mentioned projections.

Tomographical X-ray examinations can provide additional information about the condition of the ossicles (Mündnich and Frey, 1959, Langfeldt, 1963, Brünner, 1964, Valvassori, 1967). Using this technique, Andersen et al., (1962) found pathological changes in the ossicular system in 16 of 21 patients, but only 11 of these radiological examinations were fully confirmed during the subsequent operations. In all of these cases, deformities or luxations of the incus or the malleus were disclosed. On the other hand, tomographical examination was revealed to be less valuable in cases of slight dislocations or defects localized in the incudostapedial articulation. But, as it will be shown in the Clinical Report II (see below), the tomographic X-ray examination has provided increasingly accurate information on the condition of the ossicles.

7. Tympanotomia Explorativa. As it may be seen from the material noted above, it can be difficult to provide pre-operative verification of a diagnosis of a defective ossicular system, even though this condition will often be suspected.

In numerous cases, a final diagnosis can only be reached during the explorative tympanotomy.

panic membrane will often be more or less cicatricial especially the upper posterior sector of the drum Now and then it may be possible—especially with the aid of an operating microscope—to see through an atrophically translucent tympanic membrane and discern a luxation of the incudostapedial joint (Escher 1964)

Changes in the nature of the tympanic membrane in form of thickening, calcium deposits, atrophic or retracted zones will often be seen when defects in the ossicles have developed *after the ravages of otitis media.*

It should be noted that an examination of the mobility of the malleus and the tympanic membrane using Siegle's speculum, may provide information concerning the condition of the ossicles.

3 Audiometric Examination The configuration of the typical otosclerosis audiogram is well known indicating a greater conductive loss for the low frequencies than for the high frequencies. In addition, there is a drop in the bone-conduction curve at a maximum of about 2000 Hz (Carhart's Notch) The severity of the otosclerosis, and the extent to which the cochleae have been modified by it, will have a very considerable effect upon the configuration of the tone audiogram

In the case of a total disruption of the ossicular system with an intact tympanic membrane the conductive loss of hearing could theoretically amount to approximately 60 dB (Wullstein 1960) throughout the entire frequency range A hearing loss of this order is also seen now and then, no matter what the aetiology of the defective ossicles may be It must be emphasized, however that the conductive hearing loss following these middle ear diseases can vary greatly as reported by Does and Bottema (1965) They found that a less severe hearing loss than might be expected could be caused by an adhesion formed between the stapes and the long process of the incus, the handle of the malleus, and the tympanic membrane. Furthermore, they found several cases among their series of traumatically-caused ossicular defects where a perceptive high frequency hearing loss, or "dip" was displayed at C

Bauer (1964) provides the following audiometric characteristics for defects in the auditory ossicle system with an intact tympanic membrane.

1 A conductive hearing loss of approximately 50 dB in the speech-frequency range,
2 The bone-conduction and the air-conduction curves, for the greater part, follow parallel paths throughout the entire frequency range,
3 Carhart's Notch is not found in the bone conduction curve

4 Impedance Tests. Testing for changes in *the impedance of the tympanic membrane*—using an acoustic bridge (Metz, 1946) an electro-acoustic apparatus (Terkildsen and Scott Nielsen, 1960) or devices making use of the cross-coupling principle (Neergaard et al., 1965)—can occasionally provide valuable information about the state of the ossicles.

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2. Bone Fragments. Pieces of bone from the wall of the meatus and the mastoid cortex appear to be finding increased use in reconstructive auto-transplantation in the middle ear. In experiments with animals (guinea pigs and dogs), it has been demonstrated that auto-transplanted bone fragments can remain vital in the middle ear (Beck and Franz, 1961. Guilford et al., 1966). Beck and Franz (1961) have likewise demonstrated that changes in the dimensions of the bone fragments takes place so that the form may be altered and a certain amount of thickening may occur. These same authors also found that three auto-transplanted bone fragments in the middle ear were satisfactorily nourished from a histological point of view.

Kley and Draf (1965) have also demonstrated that auto-transplanted bone fragments have been covered by mucous membrane, that the internal structure has been retained and the nuclei of osteocyte cells were clearly stained in microscopic slides, and that the connective tissue filling the spaces within the bone was prolific and well vascularized. In one case, during a re-operation for otosclerosis, the author extirpated a piece of bone which had been implanted in the middle ear six years previously and which had served as *columella* between the tympanic membrane and the oval window. The bone had macroscopically retained its structure. Microscopic examination revealed that the bone was covered by a mucous membrane, and that there were osteocytes in the periphery of the bone, but not in the central part of the section. However, the central part did not show any signs of degeneration. This bone fragment could thus have continued its role as acting columella.

3. Cartilage has been used by Utech (1961) and Pfaltz and Meyer (1966) in auto-transplants, and they seem to retain their cartilaginous structure both macroscopically and microscopically. This was confirmed by Utech (1961) upon re-operation 12 months after implantation.

Smyth et al., (1967) make use of both auto-transplants and homo-transplants as prostheses in the middle ear. The homologous cartilage was acquired by resection of the nasal septum. They have found that both kinds of cartilage react identically in the middle ear of man and animal (cats). The cartilage remains normal macroscopically, while microscopic examination shows that the cartilaginous tissue lacks vital cells, but the normal mucous membrane has covered the implant.

B. *Foreign Bodies*

1. Polyethylene, Teflon, Steel, Tentalum, Gold, and Platinum

Prostheses of the above-named non-biological materials have been implanted in thousands of middle ears. According to Bennett (1963) there are no published records of the development of cancer in human patients after the implantation of plastic materials. However, fibro-sarcoma-like tumours may be seen to develop in experimental animals (rats) one to two years after the subcutaneous implantation of plastic materials (Oppenheimer et al., 1955). Hohmann et al., (1964) found that the development of such tumours depended upon the area of the plastic surface in contact with the tissue. It is their belief that the contact surfaces of the plastic prostheses implanted in the middle ear are so small as to eliminate any chance of the development of cancer.

Anthony (1963) has subcutaneously implanted pieces of the following materials, having dimensions corresponding to those of middle-ear prostheses, in an experimental subject. Polyethylene tube, teflon columella, steel wire, and tantalum wire. Histological examination eight and one half months later disclosed the presence of fibrosis surrounding all four materials. Furthermore, a slight chronic inflammation and giant-cell reaction was found around the teflon prosthesis.

Goldman et al., (1962) found, however, that teflon produced less reaction in cats' ears than did polyethylene, palladium, supramid, or steel.

SURGICAL TREATMENT

Review of the Literature

The object of surgical treatment of defects in the auditory ossicles must be to restore to the greatest extent possible, the function of the middle ear as an organ for the transformation of sound waves.

It is commonly accepted that the deciding factor in this function is the difference between the size of the effectively vibrating sector of the tympanic membrane and the size of the stapes footplate. On the other hand the leverage effects between the auditory ossicles are of very little importance when compared to the total sound pressure transformation.

The replacement of the complicated bony lever system by a single bone (columella) connecting the tympanic membrane with the oval window which is the natural construction of the ear among the birds, or by a direct connection between the tympanic membrane and the head of the stapes (myringo-stapedio-pexi) will theoretically result in a hearing loss of only 2 5 dB which is for practical purposes an insignificant loss of hearing

The immediate aim of a surgical operation will therefore in most cases, primarily be concerned with the creation of a columella between the tympanic membrane and the stapes or the stapes footplate A secondary goal will be the restoration of the normal functioning of the auditory ossicles, to that extent where this is possible

Before the reconstructive surgical treatment of the defective ossicles is described, the biological properties of the materials used for prostheses must be related

The following materials have been used in the reconstruction of the ossicles, or in the creation of a columella.

A. *Auto and Homo Tissue Transplantation Material*

1 Ossicle Fragments. The remains of the incus and the malleus are often used in the reconstruction of a defective ossicular system. Re operation has shown that auto-transplanted remains of the ossicles have been covered by mucous membrane, and that they have retained their original form. Microscopic examination has shown that there is no degeneration the ossicles retain their bone structure. Even though some of the central cancellous spaces in these ossicles may become enlarged, they contain vital connective tissue and blood filled capillaries (Hall and Rytzner 1960 Kley and Draf 1965)

Homo-transplanted ossicles (incus) have been used by House et al (1966) In 28 cases, they used the incus from patients who were operated upon for acoustic tumours. None of the transplants were complicated by infection. In one case the incus was rejected through a transplant tympanic membrane taken from the wall of the meatus. This incus may have been rejected because of a retraction of the tympanic membrane transplant. Both the macroscopic and the microscopic examination of this incus provided evidence to support the assumption that the bone was vital Pulec (1966) has also made use of homo-transplanted ossicles (incus) in 22 cases. It became necessary to re-operate three patients after some months. In each of the three cases, the incus was found to have a normal appearance and form when examined macroscopically and each was covered with mucous membrane However the microscopic examination failed to reveal any sign of living cells within the bones.

2. Bone Fragments. Pieces of bone from the wall of the meatus and the mastoid cortex appear to be finding increased use in reconstructive auto-transplantation in the middle ear. In experiments with animals (guinea pigs and dogs) it has been demonstrated that auto-transplanted bone fragments can remain vital in the middle ear (Beck and Franz, 1961 Guilford et al., 1966). Beck and Franz (1961) have likewise demonstrated that changes in the dimensions of the bone fragments takes place, so that the form may be altered and a certain amount of thickening may occur. These same authors also found that three auto-transplanted bone fragments in the middle ear were satisfactorily nourished from a histological point of view.

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Goldman et al., (1962) found, however that teflon produced less reaction in cats ears than did polyethylene, palladium, supramid, or steel.

Hough (1965) states that polyethylene can produce a slight inflammatory reaction in the mucous membrane and that necrosis of the incus may result

Koide (1965) reports that polyethylene produces a vigorous foreign-body reaction in an infected middle ear but that it is inactive in uninfected middle ears.

Schuknecht and Oleksiuk (1960) introduced the use of metal wire to otosclerotic surgery and they have demonstrated that both tantalum and steel wire are well tolerated in the middle ears of both experimental animals and in man The prostheses were covered by mucous membrane and did not produce foreign-body reactions.

Mehmke (1966) has found on using gold and platinum wire, that these materials are well tolerated in the middle ear

Reconstructive Surgery on the Defective Auditory Ossicles

Zöllner's and Wullstein's work on tympanoplastic surgery of the middle ear triggered significant interest in this type of reconstructive operation

Before these authors published only very few had attempted reconstructive surgery on the middle ear's sound transmission mechanism but since then, numerous authors have been concered with the problems arising in connection with such operations.

A significant number of suggested ossiculoplastic surgical treatments have been brought to light during the course of years.

The ossiculo-plastic operation which is selected will to a certain degree, depend upon the type and localization of the defect in the individual case being treated

The following methods of reconstructing the defective auditory ossicles will be described

1 Myringo-stapedio-pexi
2 Reposition of ossicular luxations and fractures
3 Interposition of prostheses
4 Transposition of ossicles

1 *Myringo-stapedio-pexi*

This technique restores the functional transmission of sound by establishing contact between the tympanic membrane and the head of the stapes. The technique can thus be used when the incus is defective or lacking, but the stapes is still intact and mobile. It was used as early as 1901 by Matte, but was then neglected until taken up again by Zöllner and Wullstein for use in radical operations with partly or wholly preserved tympanic membranes (Tympano-plastic Type III) Juers (1954) has made use of the term "myringo-stapedio-pexi" to designate this operation.

Numerous authors have published reports on the functional results of Type III tympanoplastic operations in cases of chronic otitis media (Zöllner 1966) but only a few have published the results of myringo-stapedio-pexi procedures used on patients with defective ossicles and an intakt tympanic membrane. Hamberger and Lidén (1958) have made use of transmeatal myringo-stapedio-pexi in 12 cases where the incus was more or less defective or dislocated and where the tympanic membrane remained intact. In nine cases, an improvement in hearing was achieved, with a threshold of hearing of 30 dB or less. It is stated that it was necessary to loosen the skin within the external meatus the annulus, and the tympanic membrane to the extent to about two thirds of the circumference in order to achieve contact between the tympanic membrane and the head of the stapes In some cases, it was necessary to sever the neck of the malleus and the tendon of the tensor tympani muscle in order to make the tympanic membrane's contact with the head of the stapes easier

Several authors (Pick, 1957 Thorburn, 1957 Williams, 1958 Bauer 1958 Hough 1959 Flisberg and Floberg, 1960 Riskær 1960 Hammond 1964 Escher 1964) have achieved good improvements in hearing using this technique. The authors mentioned have only published a single or very few cases each however

It is therefore evident that it is possible to achieve satisfactory improvement in hearing with the myringo-stapedio-pexi technique, but it is doubtful that satisfactory results can be reproduced with the required frequency. Guilford (1964) reports that in using this technique: 1. it is difficult to retain the posterior wall of the external meatus as the tympanic membrane must be brought into contact with the head of the stapes; 2. it is difficult to ensure a stable and adequate connection between the tympanic membrane and the head of the stapes; 3. it is difficult to ensure a sufficiently large air-filled space in the tympanic cavity as adhesions of the tympanic membrane to the promontory often occur. Finally he notes that a contributory cause of the inefficiency of this method can be the columella's position at the edge of the membrane. For these reasons, most authors seem to have given up myring-stapedio-pexi in favour of repositioning, interpositioning, or transpositioning methods.

2. *Reposition*

In the case of an isolated incus luxation, one of the first methods of treatment to be considered will be a repositioning. This can only be performed with expectation of improved hearing when the lenticular process can easily be brought into contact with the head of the stapes, and when the articulation between the incus and the malleus is functional or can be made to function. Several authors (Plester 1957, Gisselson, 1958, Hough, 1959, Filsberg and Floberg, 1960, Escher 1964, Does and Bottema, 1965) have reported successful repositioning of this sort, with good improvement in hearing as a result, especially in the lower frequencies (Risker 1960). But a repositioning which initially appears to have been successful is not always followed by an improvement in hearing (Does and Bottema, 1965, Bicknell, 1966) or an improvement may later retrogress (Schuknecht and Trupiano 1967). One possible explanation for this retrogression may be that the incudo-stapedial joint had not formed a sufficiently stable bond, and that the lenticular process has again lost contact with the head of the stapes. In order to stabilize the joint, Escher (1964) has made use of a little polyethylene prosthesis placed over the joint in a single case. Stabilization of the joint with a little segment of vein drawn over the joint, as described by Dietzel (1963) could possibly be expedient.

Repositioning of a dislocated malleus will presumably be successful only very rarely. Escher (1964) has reported a single case, but there was only a slight improvement in the patient's hearing.

A repositioning of a fractured and dislocated stapedial arch can infrequently be carried out successfully (Andersen and Elbrønd, 1968). In this case, which is also included as a report in a later part of this paper, the stapedial arch was luxated down to the promontory, but the stapedius tendon and the incudo-stapedial joint were partially intact. A little fragment of the footplate was fastened to the anterior crus, which was the reason for the stability of the repositioning. Normal hearing was attained.

3. *Interposition*

This term includes the insertion of auto- or homo-transplanted ossicles, pieces of bone or cartilage or prostheses made of non-biological material to bridge a defect in the ossicular system or to function as a columella.

a. In the case of a defective lenticular process, or a slight luxation which cannot be repositioned, pieces of bone (Hough, 1959, Beickert, 1962, Andersen et al., 1962, Buchheim, 1966) or pieces of cartilage (Pfaltz and Meyer 1966) can be interposed between the long process of the incus and the head of the stapes. However, the results of an interposition of pieces of bone are unreliable according to Zöllner (1966). The interposition of polyethylene tubing has been used by Sooy (1960), Hall

et al (1960) Hammond (1964) and Escher (1964) with good results, but Kley (1966) points out that in spite of the immediately good results, there is a possibility of subsequent loss of hearing due to pressure necrosis of the lenticular process and the stapes head This sort of effect has been observed by Ballantyne (1962) who on one occasion achieved a 50 dB improvement in hearing through the interposition of a little polyethylene tube between the long process of the incus and the stapes head After approximately six months hearing began to deteriorate again and after about one year approximately half of the improvement had been lost. Upon re-operation, the head and neck of the stapes were found to be necrotic. A stapedectomy according to Schuknecht's method was then performed In one case of an incus luxation which could not be repositioned, Kossner (1961) interposed between the head of the stapes and the long process of the incus a piece of polyethylene tube of such a length that the long process was pressed outward into contact with the tympanic membrane An exceptionally good improvement in the hearing function was achieved

b In the case of defects of the long process of the incus as well renewed function can be achieved through use of a steel wire prosthesis having an "eye" fitting the long process and connecting with the stapes head (Oppenheimer and Harrison 1963) The normal leverage effect can be re-established in this manner but it is noted that if the wire is pressed too tightly around the long process and the stapes head there may be necrosis and the prosthesis may then slip out of position. There are no reports of the results achieved with this method The "phonograph" type of prosthesis (a steel wire with an "eye" loop is fastened to the long process, and the other end inserted into the excavated head of the stapes) has been reported to give good results (Oppenheimer and Harrison 1963) Combinations of polyethylene and steel wire are also used for the repair of defects of this type (Harrison and Shambaugh 1959) It is stated that these types of prostheses are especially effective in the relatively low frequency range, but there is no mention of observation periods. These prostheses will presumably be extremely difficult to install in a satisfactory manner

Mehmke (1966) makes use of gold and platinum wire prostheses in a similar manner He additionally describes a gold clip which can be pressed down over the long process and the head of the stapes in cases of a defective lenticular process. Polyethylene tube prostheses which can be pushed up over the defective long process, and with the other end in contact with the stapes head—if necessary this end of the tube may be bent so that it will fit over the stapes head—have been used by Harrison and Shambaugh (1969) Sooy (1960) and Oppenheimer and Harrison (1963) with at least initially good results. In addition to the difficulty experienced in inserting these prostheses, it must be expected that they can produce necrosis of the long process and the head of the stapes. This author has observed such a necrosis of the long process of the incus after the insertion of a polyethylene-tube prosthesis (Elbrønd and Elpern 1965)

In cases where the long process of the incus is lacking a columella effect can be achieved by interposing a prosthesis between the head of the stapes and the tympanic membrane or the handle of the malleus. A method reported by numerous authors to be suitable for the creation of such a columella effect is the interposition of the body of the incus between the stapes head the handle of the malleus, and the tympanic membrane (Andersen et al., 1962 Portmann 1963 Guilford 1964 1966 House and Sheehy 1963 Steffen 1964 Chandler 1965 Sheehy 1965 Perrét, 1966 Smyth et al. 1967)

The first to have used auto-transplanted incus (and malleus head) were Hall and Rytzner (1957)

Guilford (1966) makes use of the following technique The incus is extracted and inspected. Thereafter the incus is replaced in the middle

ear so that the previously lateral surface now rest on the head of the stapes. Should there be a stump of the lenticular process still affixed to the stapes head, this fragment is removed first, in order to secure the best possible contact surface for the incus. The apex of the short process is positioned under the handle of the malleus with the shortened long process lying parallel with the handle. The incus is supported in this position with spongostan. Finally the tympanic membrane is tamponed into contact with the incus. In 28 cases where this technique was used, an average hearing improvement of 23.2 dB was achieved, and 86.5 per cent of these patients achieved a threshold of hearing of 30 dB or better. However myringo-plastic operations had been performed in at least a part of this group. House and Sheehy (1963) also report that they have achieved the best results by interposing the incus between the stapes, the handle of the malleus, and the tympanic membrane. Smyth et al., (1967) report that in 70 per cent, or 85 ears, where this technique was attempted, the air-bone gap was reduced to 10 dB or less.

c In cases where the incus totally lacking, the excised head of the malleus can be interposed between the head of the stapes, the malleus handle and the tympanic membrane (Portmann, 1963 Mehmke, 1964 Sheehy 1965)

The columella interposition of shaped bone fragments between the stapes head and the handle of the malleus, or between the stapes head and the tympanic membrane, was used by Zöllner (1960), especially in cases where conditions were not suitable for a myringo-stapedio-pexi. By interposing the shaped bone fragment as described by Zöllner (he calls this a columellization") it is possible to avoid the flat tympanic cavity and resultant difficulties which follow a myringo-stapedio-pexi. Zöllner (1960) has additionally described a technique for excising bone columella of the optimal shape and size from the cortex of the mastoid process. Others as well (Andersen et al 1962 Sheehy 1965 Bauer 1966) have successfully made use of a bone columella in treating defects of this type. With this technique, Bauer (1966) has secured an average improvement in hearing of 23 6 dB in a group of 16 patients. However these patients had also been treated with myringo-plastic operations using fascia.

The interposition of pieces of cartilage has been used by Utech (1961) and Pfaltz and Meyer (1966) in defects of this type, with good results.

Polyethylene and teflon prostheses with various shapes (see below) can be interposed between the head of the stapes and the tympanic membrane (Sheehy 1965 Austin, 1965) or between the head of the stapes and the handle of the malleus (Does and Bottema, 1965) with relative ease, but a not insignificant percentage of the cases where the prosthesis is placed against the tympanic membrane will sooner or later result in a perforation at this point. Guilford (1964) has used teflon prostheses from the head of the stapes to the tympanic membrane, or a transplant, in 17 cases. He achieved an average improvement in hearing of 9 7 dB. The series is skewed, however by one case having a hearing loss of 35 dB

When the incus is defective, or totally lacking, Gundersen (1964) has used an incus prosthesis, i. e. an accurate polyethylene model of a normal incus. This polyethylene incus is held in place with a little steel clip which grips the neck of the malleus. The articulation with the head of the stapes is ensured by use of a little polyethylene tube. Should the stapedial arch be lacking, the polyethylene tube can be extended to articulate with the stapes footplate. Gundersen (1964) has used this prosthesis in 20 cases. He states that the results, in regard to improvement in hearing, have been encouraging, but he provides no other results.

Metal wire prostheses (tantalum, steel, gold, or platinum) connecting the handle of the malleus to the head of the stapes (malleolo-stapedio-pexi) have been used by Oppenheimer and Harrison (1963) and Mehmke (1966)

et al (1960) Hammond (1964) and Escher (1964) with good results, but Kley (1966) points out that in spite of the immediately good results, there is a possibility of subsequent loos of hearing due to pressure necrosis of the lenticular process and the stapes head This sort of effect has been observed by Ballantyne (1962) who on one occasion achieved a 50 dB improvement in hearing through the interposition of a little polyethylene tube between the long process of the incus and the stapes head After approximately six months, hearing began to deteriorate again, and after about one year approximately half of the improvement had been lost. Upon re-operation, the head and neck of the stapes were found to be necrotic. A stapedectomy according to Schuknecht's method was then performed In one case of an incus luxation which could not be repositioned Kossner (1961) interposed between the head of the stapes and the long process of the incus a piece of polyethylene tube of such a length that the long process was pressed outward into contact with the tympanic membrane An exceptionally good improvement in the hearing function was achieved

b In the case of defects of the long process of the incus as well renewed function can be achieved through use of a steel wire prosthesis having an "eye" fitting the long process and connecting with the stapes head (Oppenheimer and Harrison, 1963) The normal leverage effect can be re-established in this manner but it is noted that if the wire is pressed too tightly around the long process and the stapes head there may be necrosis and the prosthesis may then slip out of position There are no reports of the results achieved with this method The "phonograph" type of prosthesis (a steel wire with an "eye" loop is fastened to the long process, and the other end inserted into the excavated head of the stapes) has been reported to give good results (Oppenheimer and Harrison, 1963) Combinations of polyethylene and steel wire are also used for the repair of defects of this type (Harrison and Shambaugh, 1959) It is stated that these types of prostheses are especially effective in the relatively low frequency range but there is no mention of observation periods. These prostheses will presumably be extremely difficult to install in a satisfactory manner

Mehmke (1966) makes use of gold and platinum wire prostheses in a similar manner He additionally describes a gold clip which can be pressed down over the long process and the head of the stapes in cases of a defective lenticular process. Polyethylene tube prostheses which can be pushed up over the defective long process, and with the other end in contact with the stapes head—if necessary this end of the tube may be bent so that it will fit over the stapes head—have been used by Harrison and Shambaugh (1969) Sooy (1960) and Oppenheimer and Harrison (1963) with at least initially good results. In addition to the difficulty experienced in inserting these prostheses, it must be expected that they can produce necrosis of the long process and the head of the stapes. This author has observed such a necrosis of the long process of the incus after the insertion of a polyethylene-tube prosthesis (Elbrønd and Elpern 1965)

In cases where the long process of the incus is lacking, a columella effect can be achieved by interposing a prosthesis between the head of the stapes and the tympanic membrane or the handle of the malleus. A method reported by numerous authors to be suitable for the creation of such a columella effect is the interposition of the body of the incus between the stapes head, the handle of the malleus, and the tympanic membrane (Andersen et al., 1962 Portmann, 1963 Guilford, 1964 1966 House and Sheehy 1963 Steffen, 1964 Chandler 1965 Sheehy 1965 Perrét, 1966 Smyth et al 1967)

The first to have used auto-transplanted incus (and malleus head) were Hall and Rytzner (1957)

Guilford (1966) makes use of the following technique The incus is extracted and inspected Thereafter the incus is replaced in the middle

body prostheses in the middle ear (Wullstein, 1960)

Similar experiences have been recorded by numerous authors (Brockman, 1961 Hayden, 1961 Plester 1961 Seidentop and Brown, 1966) This continues to be true even where the protheses are given such a shape as to greatly reduce the tendencies toward perforation of the tympanic membrane or transplant, e.g. sunflower" or "wire-mesh" prostheses (House and Sheehy 1963 Sheehy 1965)

On the basis of the experiences gained from several hundred operations, Portmann (1967) reports achieving good immediate results following the introduction of polyethylene or teflon, but if these prostheses were inserted in direct contact with the tympanic membrane they were expelled in nearly every case.

Austin (1965) has used teflon prostheses interposed between the stapes footplate and the handle of the malleus in a large number (338) of cases. These prostheses are provided with an "eye in one end, to permit fastening around the handle. The other end rests on the footplate. In order to make possible the use of this type of prosthesis in cases where the stapedial arch remains intact, Austin (1965) often removes it. He reports that in 63 per cent of 134 cases, this technique has resulted in reductions of the air-bone gap to less than 10 dB. Three per cent of the prostheses were expelled, and 1.8 per cent slipped out of position. Guilford (1964) has used the same type of prosthesis in ten cases with an average improvement in hearing of 24 1 dB. Guilford (1964) draws attention, however to the existing risk of displacement of the stapes footplate when attempting to achieve a satisfactory positioning of the prosthesis while simultaneously retaining the optimal length of the prosthesis. He consequently uses prostheses which are slightly shorter than the distance from the handle of the malleus to the footplate of the stapes, and compensates for the difference by placing small wedge-shaped pieces of bone or tantalum between the prosthesis and the footplate. In addition to the length adjustment, the wedge also reduces the tendency of the somewhat diagonally-positioned prosthesis to slip backwards on the footplate.

Sheehy (1965) uses steel wire prosthesis (IRP- Incus Replacement Prosthesis) which can be fastened to the handle of the malleus and which can reach the stapes footplate. Using this type of prosthesis, and with polyethylene tube from the malleus to the footplate, he has in 70 per cent of the cases obtained an air bone gap of 20 dB or less, four months after operating. Tabb (1963) has used teflon-coated steel wire prostheses from the stapes footplate to the handle of the malleus or the tympanic membrane. Mehmke (1966) has used metal wire (of gold or platinum) in a similar manner from the handle of the footplate, and reports achieving good results.

4 *Transposition*

Transposition is the re-arrangement of ossicles while wholly or partially preserving their suspensory ligaments, articulations, and muscle insertions. In cases of defects in the incus, Wustrow (1957) has been able to turn the handle of the malleus sufficiently to bring it into contact with the head of the stapes. The tympanic membrane must first be dissected free of the handle, and the head of the malleus must often be removed, but the tendon of the tensor muscle and the ligaments of the malleus are preserved intact. He states that the primary indication for carrying out a reconstruction of the ossicular system in this manner is the avoidance of the flat tympanic cavity which follows Type III tympano-plastic and myringo-stapedio-pexi, and which involves a significant risk of adhesions between the tympanic membrane and the transplant, or the promontory He gives no results.

Hall and Rytzner (1957), who have used auto-transplantation of the malleus and the incus in otosclerosis operations and with defects in the ossicular system since 1955 have also described transposition of the malleus in connection with defects of the incus and the stape

d In the case of an isolated defect in the stapes or a fracture of the stapes crura, where the remainder of the ossicular system remains functional one of the prosthetic substitutes for the stapes used in connection with stapedectomy (Kley 1966) may serve without the removal of the footplate of the stapes In two cases of fracture of the stapes, Sadé (1964) has preferred to carry out a stapedectomy according to Schuknecht s method—using a steel wire prosthesis—with good results. Robinson (1961) has also achieved a good result in a case where he performed a stapedectomy according to Shea s method, with the interposition of polyethylene tubing.

Hammond (1964) has made use of platinectomy covering the oval window with a piece of vein followed by interposition of the stapedial arch. Does and Bottema (1965) have interposed connective tissue between the stapedial arch and the stapes footplate, in a case where the stapes crura were fractured at the footplate whereby the air bone gap was reduced from 45 dB to 15 dB In a case where the crura were fractured during an attempt to mobilize an otosclerotic footplate Meyers (1959) stabilized the fracture with a thin polyethylene tube on the crura The immediate result was good

e If the stapedial arch and the tip of the long process of the incus are lacking a columella effect can be achieved by interposing the incus between the handle of the malleus and the stapes footplate or between the tympanic membrane and the footplate (Austin 1965 Sheehy 1965 Chandler 1965) As pointed out by Chandler (1965) and Austin (1965) the length of the incus from the apex of the short process to the middle of the saddle shaped surface of the articulation is often very nearly the distance from the footplate to the handle of the malleus, so that the incus can be repositioned with the short process on the footplate, and with the handle resting in the saddle shaped articular surface If the incus is unstable in this position, small pieces of connective tissue can be positioned around the short process at the footplate.

f In cases where the incus and the stapedial arch (and perhaps the handle of the malleus as well) were totally lacking, Zöllner (1960) and Guilford (1966) have made use of shaped pieces of bone interposed between the footplate and the handle of the malleus. These bone prostheses are provided with notches which fit the handle, thus ensuring positive and stable contact Bauer (1966) has used bone fragments interposed between the footplate and the tympanic membrane—or a transplant serving as the tympanic membrane—in eight patients. The improvement in hearing averaged 25 3 dB Two of these patients suffered post-operative infections in the ear but in spite of the infections, the bone transplants were not expelled.

In a similar manner Utech (1961) has made use of cartilage pieces from the auricle Using pieces of cartilage with attached perichondrium from the tragus Brockman (1965) has altered 30 cases of Type IV tympano-plastic to Type III He achieved an average improvement in hearing of 16 6 dB Only four patients did not display any improvement. In only one case there was a partial degeneration of the transplant. Smyth et al., (1967) make use of homologue pieces of cartilage shaped like a boomerang with one end on the footplate of the stapes and with the lateral end shoved in under the handle of the malleus or where the handle is lacking with support at the distal edge of the annulus. They report that this type of prosthesis has reduced the air bone gap to 10 dB or less in 71 per cent of these cases.

Reconstruction of this type of defect is often attempted with prostheses made of 'foreign-body materials. Wullstein (1956) has attempted to use acrylic prostheses to alter Type IV tympano-plastic to Type III He reports that he has had some good results from the use of this kind of artificial columella, but he found that they had a tendency to perforate the newly-formed tympanic membrane, for which reason he has since given up the use of foreign-

6. Interposition and transposition methods often produce good results.

7. An evaluation of tabulations of hearing improvements with the object of deciding whether one method or reconstruction is statistically better than another is not quite possible. There are too many variable factors which can influence the reported results, such as the choice of patients, weighing of the indications, surgical experience and technique, the use of local or general anaesthesia, the method of registering the results, the period of observation, etc. It is a question of factors which are often not mentioned.

However the literature survey seems to indicate, in general, that the results of the operations, especially in regard to the permanency of the hearing improvements achieved, have shown betterment in recent years. This seems to be especially true since the remains of ossicles, pieces of bone, and cartilage have increasingly been used as prosthetic materials.

Hearing improvements after reconstructive surgery on the defective auditory ossicle system are not yet fully satisfactory nor are they quite on a par with the results achieved with otosclerosis surgery

dial arch The malleus is mobilized by severing the tendon of the tensor muscle and the ligaments, the handle is dissected free of the tympanic membrane except at the umbo and the *malleus can then be rotated so that the head fits into the oval niche*

Miodonski (1959 cit by Proctor 1961) has used the following technique After resection of the head of the malleus, the distal end of the handle is dissected free of the tympanic membrane The handle can then be rotated so that *the umbo can be brought into contact with the head of the stapes.*

Rubinstein et al (1962) mobilize the malleus by dissecting it free of the tympanic membrane and severing all of the ligaments, so that the malleus is fixed only by the tendon of the tensor muscle The malleus can now be rotated at will, so that either the head or the end of the handle of the malleus can be brought into contact with the head of the stapes They have used this technique on 14 patients Of these 12 demonstrated hearing improvements of more than 15 dB the average for these 12 being 28 5 dB and the post-operative air bone gap averaged 12 dB

Kley (1964 and 1966) also used transposition of the malleus in cases where the incus is defective or lacking. In Malleolo-stapedio-pexi I the head of the malleus is excised directly above the insertion of the tendon of the tensor muscle. The distal part of the handle is dissected free of the tympanic membrane, so that is can be turned and the umbo is then brought into contact with the head of the stapes. In Malleolo-stapedio-pexi II the neck of the malleus is severed just under the insertion of the tendon of the tensor muscle. The head of the malleus is then rotated about the tendon of the tensor muscle until it comes to rest on the head of the stapes.

On rare occasions, where the lenticular process of the incus is defective the incus can be rotated about the posterior ligament of the short process of the incus so that the long process can be brought into contact with the head of the stapes (Zöllner 1955 Farrior 1960)

A necrosis of the lenticular process of the incus can now and then be corrected by tipping the stapes in the oval niche, in the proximal direction so that the head of the stapes contacts the long process. Sadé (1965) has attempted this on seven patients. This slight transposition of the stapes and the resulting contact with the long process of the incus was maintained by placing small wedge-shaped bone fragments in the opening between the stapes and the promontory Hearing improvement *was obtained in six of the cases (averaging about 30 dB)*

Farrior (1960) has described transposition of the incus in defects of the long process and the stapedial arch. The short process of the incus was loosened and brought into contact with the stapes footplate without loosening the *articulation between the incus and the malleus.* Farrior has also made use of malleus transposition.

Conclusions

On the basis of this survey of the literature, it is possible to establish that

1 Prostheses of plastic materials, in most cases, are unsuitable for reconstruction of the defective ossicular system, at least in those cases where the prosthesis is in direct contact with the tympanic membrane Only rarely is there a lasting improvement in hearing when this type of prosthesis is used

2 Prostheses of tissue (bone or cartilage) are satisfactory and can produce lasting im*provements in hearing*

3 Prostheses of metal wire are satisfactory when they can be fastened around or press against the remnants of the ossicular system

4 Myringo-stapedio-pexi does not seem to provide satisfactory or lasting improvements in hearing with sufficient frequency

5 Repositioning of dislocated ossicles can now and then produce satisfactory results, but it can be difficult to preserve the reduction, once obtained.

6. Interposition and transposition methods often produce good results.

7 An evaluation of tabulations of hearing improvements with the object of deciding whether one method or reconstruction is statistically better than another is not quite possible. There are too many variable factors which can influence the reported results, such as the choice of patients, weighing of the indications, surgical experience and technique, the use of local or general anaesthesia, the method of registering the results, the period of observation, etc. It is a question of factors which are often not mentioned.

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CLINICAL REPORT I

Clinical Series I consists of 67 patients who have been operated upon for defects of the auditory ossicle system Four of these patients have recieved surgery in both ears. The series thus covers a total of 71 ears.

All of the patients have had intact tympanic membranes, although these were often cica trized and the middle ear was air filled. The requirement of an intact tympanic membrane was due to the desire for a group of patients where the improvement in hearing (or perhaps the hearing loss) was primarily due to the re constructive operation on the defective ossicular system

The distribution of the patients in respect to age and sex can be seen in table No 1

Table I

Age	Men	Women	Total	Percent age
5–14	10	8	18	7
15–24	7	5	1	18
25–34	9	6	15	
35–44	7	2	9	14
45–54	6	1	7	10
55–64	3	3	6	9
Total	*42*	*25*	*67*	*100*

Examinations

All of the patients have undergone the usual *oto-rhinolaryngological examination,* including tone audiometry and tuning-fork tests

Regarding special tests, it can be mentioned that qualitative impedance measurements, with efforts to register the stapedius reflex, have been performed in 50 cases. Most of the im pedance measurements have been performed with an acoustical bridge, according to the method of Metz (1946) Only a few impedance measurements were made by the cross-coupling method of Neergaard et al., (1965) In most of these cases (46) it was naturally impossible to demonstrate any stapedius reflex, as any change in the impedance resulting from a contraction of the stapedius muscle would necessitate an intact and mobile ossicular system. In a couple of cases, weak stapedius reflex reactions were detected, in spite of defects in the ossicular system (absence of the long process of the incus) During the subsequent oper ations, adhesions from the stapes to the handle of the malleus and the tympanic membrane were found, thus explaining these reactions. Two cases, where the cross-coupling method of impedance measurement was used, will be described to illustrate how an impedance measurement can contribute to the diagnosis of a stapes fracture.

The first patient is a 44-year-old man who, at the age of 16 years, suffered a cranial trauma with bleeding from the left ear but no loss of consciousness. From that time on, the patient had a severe loss of hearing in the left ear together with a strongly-ringing tinnitus. Audiometry indicated an air bone gap of about 50 dB The impedance test indicated normal pressure in both middle ears. In the left ear a perceptable reflex was triggered by contra lateral stimulation, but no reflex resulted from homolateral stimulation. In the right ear only homolateral stimulation triggered the reflex. Tensor reflexes could not be detected. The examination thus suggested an interruption of the ossicular system medial to the insertion of the stapedius muscle on the head of the stapes. The operation disclosed that the stapedial arch was fractured and luxated so that the crura

rested on the promontory The joint between the incus and the stapes was still intact, and the insertion of the tendon of the stapedius muscle was found to be normal. A small fragment of the footplate was still fastened to the anterior crus, which made possible a stable repositioning of the fractured stapedial arch. Post-operative testing revealed that the air bone gap had been reduced to 5 dB (Diagram No. 3 Case 8), and that a stapedius reflex could be demonstrated with homolateral stimulation of the left ear although it was weaker than in the right ear

In another case the cross-coupling method demonstrated a stapedius reflex and a stronger tensor reflex in the relevant ear The patient was a 28-year-old man who had suffered a cranial trauma 13 years before. The operation disclosed a fracture of the stapedial arch. A polyethylene tube was interposed between the long process of the incus and the stapes foot plate (Diagram No. 3 Case 6).

X-ray examinations of the ear were performed in 57 cases, using the conventional projections (Schüller's, Stenver's, and the Chausse III) In only a few cases did these radiographs provide information leading to a suspicion of a defective or luxated ossicle. In 41 cases, the X-ray examination was supplemented with tomographic examination, using the Polytome in both the frontal and sagittal planes, as a rule. There was good agreement between the radiological and the surgical disclosures in 20 cases.

Only a few individual patients were given tuba function examinations in the form of catheterization of the Eustachian tube Many of the patients, however had been treated with tuba catheterization or air inflation, according to Politzer's method, for varying periods prior to admission to hospital.

Table 2. *Distribution According to Aetiology*

	Total	Men	Women
Post-infectious	28	15	13
Cholesteatomal	1		1
Post-traumatic	36	24	12
(cranial)	21	14	7
(operative)	11	8	3
(transmeatal)	4	2	2
Congenital	1		1
Radiological	1	1	
Unknown	4	3	1
Total	71	43	28

Surgical Evidence

Five of the patients in the post-infectious group of 28 could not give any information about previous occurance of otitis media or any other cause of the loss of hearing, but these cases have been tabulated as post-infectious because of cicatrized tympanic membranes like those found after otitis media. In 22 cases, surgery disclosed that the lenticular process and the long process of the incus were absent to a greater or lesser degree, sometimes replaced by a fibrous cord, but that the stapes were intact. In the six remaining cases, the stapedial arch was more or less defective, and in five of these cases, it was not possible to find any trace of the incus.

In one case (an 11-year-old girl) a little cholesteatoma was found behind an intact tympanic membrane The cholesteatoma had caused the atrophy of the long process of the incus and the crura of the stapes. There was no history of otitis media, paracentesis, or similar condition which could explain the presence of the cholesteatoma. It must therefore be considered to have been a primary cholesteatoma.

Among the 21 cases of hearing losses resulting from cranial traumata, bleeding from the ear is recorded in the journals of 18 of the patients, and in three cases leakage of cerebrospinal fluid is also recorded as having persisted for periods of varying duration. Four of these patients experienced temporary facial paralysis.

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In ten cases, the incus was found to be more or less luxated and in three cases, the incus could not be located A fracture of the handle of the malleus occured with the incus luxation in two cases Fractures of the stapes crura sometimes with attendant dislocation of the stapedial arch were found in eight patients In seven of these cases, only the stapes were found to be fractured. In the remaining case, the incus was additionally found to be luxated out of the field of vision

The 11 post-operative traumata tabulated above refer to hearing losses after mastoidec tomy during childhood The incus was found to be luxated to various degrees in five of these cases, while the incus was not observed at all in the remaining six patients.

In four cases, the hearing loss had followed traumata through the external meatus The objects directly responsible for the traumata were a paracentesis needle, a hair clip a twig, and a straw The operations disclosed fractures of the stapes crura in two cases, and in the last two cases, the long process of the incus and the stapes crura had necrotized away although the head of the stapes was present in both of these cases, still fastened to the stapedius tendon. It must be assumed that the immediate injuries in both of these cases were fractures of the long process and the stapes crura resulting in an insufficient supply of blood except for the head of the stapes

In one case—a girl of nine years—the cause of the hearing loss is tabulated as congenital The patient was an identical twin (the other had died at birth) and had an asymmetrical face The auricle on the side having the defective hearing was smaller than the auricle on the other side In addition, there was a pre auricular fistula. X ray examination disclosed characteristic features of Franceschetti s Syn drome The operation showed the incus to be deformed an^d without connection with the stapes The [illegible] was also found to be fixed in the epity[illegible] [illegible]ic recess It was mobilized, excised, an[illegible] [illegible] t[illegible]rposed between the stapes and the tympanic membrane

One case is tabulated as having developed after radiological treatment. The patient was a boy of 14 years, who two years previously had received radiation treatment for a reticular sarcoma in the rhino-pharyngeal region. Sur gery revealed the long process of the incus to have been replaced by a fibrous cord. An attempt was made to extract the remains of the incus, but the body of incus was found to be in an advanced stage of halisteresis, and crumbled away completely as the extraction was attempted.

Four patients are registered under the head ing 'unknown" In these cases, there are no clues suggesting otitis media cranial traumata, or any of the other listed causes of hearing losses. Otoscopic examination showed normal tympanic membranes, and the patients explain that the hearing losses have gradually accumulated over a period of years. In two of these cases, the long process of the incus was found to have been replaced by a fibrous cord. In the other two cases, the stapes crura were found to have been replaced by a similar fibrous cord. Microscopic examination of the remnant of the stapes in one of these cases revealed a struc tureless area where the lacunae ossium were empty without activity of osteoblasts and osteoclasts.

Treatment and Results

The treatment in all cases has consisted of ossicular plastic surgery using a transmeatal approach to the middle ear according to Rosen s method. General anaesthesia has been used in 49 of the operations, the remainder being performed under local anaesthesia. As previously mentioned, the series consists of 71 ears, but a total of ten re-operations have been carried out, so that the results of 81 opera tions in all must be described

The character of the ossicular plastic surgery to a certain extent, has been dependent upon the state of the ossicular system in each in dividual case.

In order to reach some judgement of the

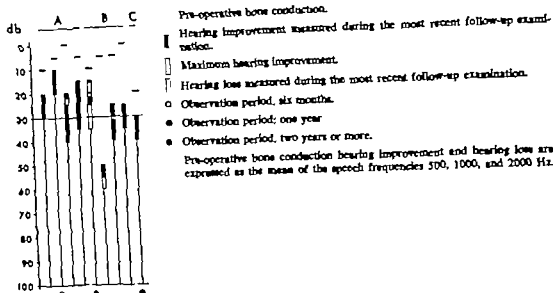


Diagram No. 1 Series I, Group 1

A. Nos 1–4. Interposition of a bone fragment between the head of the stapes and the long process of the incus.
B. Nos. 5–8. Interposition of a polyethylene tube between the head of the stapes and the long process of the incus.
C No. 9 Reposition of luxation of the incudo-stapedial articulation.

influence of the operational technique and the state of the ossicles on the ultimate results, it has consequently been felt desirable to separate the series into groups according to the type of defect, and its site in the ossicular system.

1 Necrosis and fracture of the lenticular process of the incus and luxation of the incudo-stapedial articulation.

2. Partial or total absence of the incus, and dislocation of the incus.

3 Necrosis or fracture of the stapedial arch.

4 Partial or total absence of the incus, combined with a defect in the stapedial arch.

As it may be seen in Diagrams Nos. 1 2 3 and 4 associated with each of these groups, the following information is tabulated for each operation.

A. Improvement or loss of hearing, expressed as the mean of the speech frequencies 500 1000 and 2000 Hz recorded during the most *recent follow*-up test.

B The maximum improvement in hearing, expressed as the arithmetic mean of the above mentioned speech frequencies. This is determined, as a rule, one to three months after the operation. By comparing the values of Point A and Point B the amount of hearing loss during the observation period can be determined.

C. The arithmetic mean of the pre-operative bone-conduction hearing ability at the speech frequencies 500 1000 and 2000 Hz.

1 Necrosis and fracture of the lenticular process of the incus and luxation of the incudo-stapedial articulation.

This group, consisting of nine operations (one of which was a re-operation) where reconstruction of the normal ossicular function has been attempted by 1 Interposition of

In ten cases, the incus was found to be more or less luxated, and in three cases, the incus could not be located. A fracture of the handle of the malleus occured with the incus luxation in two cases. Fractures of the stapes crura, sometimes with attendant dislocation of the stapedial arch were found in eight patients. In seven of these cases, only the stapes were found to be fractured. In the remaining case, the incus was additionally found to be luxated out of the field of vision

The 11 post-operative traumata tabulated above refer to hearing losses after mastoidectomy during childhood The incus was found to be luxated to various degrees in five of these cases while the incus was not observed at all in the remaining six patients.

In four cases, the hearing loss had followed traumata through the external meatus The objects directly responsible for the traumata were a paracentesis needle a hair clip a twig, and a straw The operations disclosed fractures of the stapes crura in two cases, and in the last two cases, the long process of the incus and the stapes crura had necrotized away although the head of the stapes was present in both of these cases, still fastened to the stapedius tendon. It must be assumed that the immediate injuries in both of these cases were fractures of the long process and the stapes crura, resulting in an insufficient supply of blood except for the head of the stapes.

In one case—a girl of nine years—the cause of the hearing loss is tabulated as congenital. The patient was an identical twin (the other had died at birth) and had an asymmetrical face. The auricle on the side having the defective hearing was smaller than the auricle on the other side In addition, there was a preauricular fistula X ray examination disclosed characteristic features of Franceschetti's Syndrome The operation showed the incus to be deformed and without connection with the stapes. The incus was also found to be fixed in the epitympanic recess. It was mobilized, excised, and interposed between the stapes and the tympanic membrane.

One case is tabulated as having developed after radiological treatment. The patient was a boy of 14 years, who two years previously had received radiation treatment for a reticular sarcoma in the rhino-pharyngeal region. Surgery revealed the long process of the incus to have been replaced by a fibrous cord. An attempt was made to extract the remains of the incus but the body of incus was found to be in an advanced stage of halisteresis, and crumbled away completely as the extraction was attempted

Four patients are registered under the heading "unknown" In these cases, there are no clues suggesting otitis media cranial traumata, or any of the other listed causes of hearing losses. Otoscopic examination showed normal tympanic membranes, and the patients explain that the hearing losses have gradually accumulated over a period of years. In two of these cases, the long process of the incus was found to have been replaced by a fibrous cord. In the other two cases, the stapes crura were found to have been replaced by a similar fibrous cord. Microscopic examination of the remnant of the stapes in one of these cases revealed a structureless area where the lacunae ossium were empty without activity of osteoblasts and osteoclasts.

Treatment and Results

The treatment in all cases has consisted of ossicular plastic surgery using a transmeatal approach to the middle ear according to Rosen's method General anaesthesia has been used in 49 of the operations, the remainder being performed under local anaesthesia. As previously mentioned, the series consists of 71 ears, but a total of ten re-operations have been carried out, so that the results of 81 operations in all must be described.

The character of the ossicular plastic surgery to a certain extent, has been dependent upon the state of the ossicular system in each individual case.

In order to reach some judgement of the

cases) or polyethylene tube (seven cases) between the head of the stapes and the tympanic membrane has also been carried out.

In one case, a polyethylene tube with a flare has been interposed between the head of the stapes and the handle of the malleus.

Myringo-stapedio-pexi has been performed in two additional cases.

The patient listed as Case 11 has been reoperated and listed again as Case 12. During the first operation, the incus was found to be significantly dislocated. The incus was then placed in contact with the stapes head, to form a columella. Upon re-operation, it was disclosed that the connection between the body of the incus and the stapes head was quite loose. This articulation was improved by creating a little excavation in the body of the incus, to accept the head of the stapes. The short process of the incus was interposed under the handle of the malleus.

One year after the operation, the flare of the polyethylene tube was observed to have partially perforated the tympanic membrane in the case listed as Case 35. In order to reduce the possibility of tympanic-membrane perforation by the polyethylene tube, the chorda tympani was placed between the prosthesis and the tympanic membrane in Case 40 and in Case 36 a little piece of bone was placed between the flared polyethylene tube and the tympanic membrane.

The results are tabulated in Diagram 2.

3 Necrosis or fracture of the stapedial arch. This group consists of eight operations, where the normal ossicular effect has been sought reconstructed, partly by the interposition of polyethylene tube between the stapes footplate and the long process of the incus (six cases), and partly by the reduction of a fractured and dislocated stapedial arch (two cases). Two of these cases have already been described (Cases 6 and 8 see page 25)

The patient tabulated as Case 4 has been re-operated. During the first operation, a polyethylene tube was positioned between the footplate and the long process of the incus. Upon re-operation, this prosthesis was replaced by interposing the incus between the footplate and the tympanic membrane, for which reason this re-operation is included in Group 4 (Diagram 4 Case 4)

The results are tabulated in Diagram 3

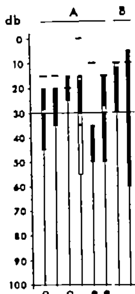


Diagram No. 3. Series I, Group 3

A. Nos. 1–6. Interposition of polyethylene tube between the long process of the incus and the footplate of the stapes.
B. Nos. 7–8. Reposition of a fractured and dislocated stapedial arch.

4 Partial or total absence of the incus, combined with a defect in the stapedial arch. Group No. 4 consists of 20 operations (including seven re-operations) In this group, a columella effect has been sought through the interposition of bone fragments (four cases) polyethylene tube (seven cases) or the incus (six cases) between the stapes footplate and the tympanic membrane.

In Cases 7 8, and 9 interposition was attempted using the head and neck of the malleus, supplemented by a little piece of bone. Actually these three cases are made up of one patient who has been re-operated twice. In the final re-operation (Case 9), an attempt was

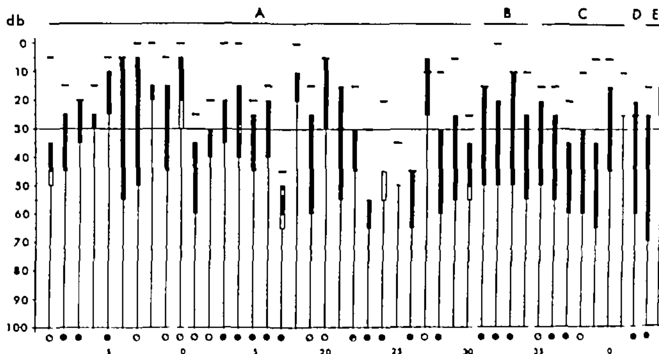


Diagram No. 2. Series I Group 2.

A Nos. 1–30. Interposition of the body of the incus between the head of the stapes and the tympanic membrane
B. Nos. 31–34 Interposition of a bone fragment between the head of the stapes and the tympanic membrane.
C. Nos. 35–41 Interposition of a polyethylene tube between the head of the stapes and the tympanic membrane
D No. 42 Interposition of a polyethylene tube between the head of the stapes and the handle of the malleus.
E. Nos. 43–44 Myringo-stapedio-pexi

pieces of bone or polyethylene tube traversing the defect from the head of the stapes to the long process of the incus (eight cases) 2 *Repositioning of a luxation of the incudo-stapedial articulation* (one case)

The results obtained are tabulated in Diagram No 1 where Case 4 is the result of the re-operation of Case 7 In the first operation, a polyethylene tube was interposed between the head of the stapes and the long process of the incus. Upon re-operation, the polyethylene tube was found to have slipped off the long process of the incus so that it contacted the tympanic membrane, where there was a little perforation. The patient was then re-operated, and a little piece of bone interposed in the defect, but this didn t result in any improvement in hearing, and the patient has since been re-operated twice (Diagram 4 Cases 5 and 6) During the re-operation of Case 8 (Diagram No 1) it was observed that the polyethylene tube interposed between the head of the stapes and the long process of the incus had produced additional necrosis of the latter ossicle The polyethylene tube was consequently removed and the body of the incus itself was interposed between the head of the stapes and the tympanic membrane, with a good improvement in hearing as a result (Diagram No 2 Case 27)

2 Partial or total absence of the incus, and dislocation of the incus.

In this group of 44 operations (including two re-operations) attempts have been made to achieve a columella effect in 30 cases by *interposing the body of the incus between the head of the stapes, the handle of the malleus, and the tympanic membrane.* No special effort has been made to secure contact between the incus and the handle of the malleus.

The interposition of bone fragments (four

Table 3

	Quantity	Arithmetic mean increase in hearing	Number of cases at or above specified level		Post-operative air-bone gap		
		dB	20 dB level	30 dB level	10 dB or less	15 dB	20 dB
Group No. 1 Defective lenticular process, luxation of the incudo-stapedial joint	9	5 (12)	1	6	2	3	3
Group No. 2 Partial or complete absence of the incus, luxation of the incus	44	18 (22)	15	30	18	27	35
Interposition of the incus between the head of the stapes and the tympanic membrane	30	13 (19)	8	18	12	18	23
Group No. 3 Necrosis or fracture of the stapedial arch	8	14 (24)	3	6	3	6	6
Group No. 4 Partial or complete absence of the incus combined with defective stapedial arch	20	4 (11)	1	6	5	7	8

The mean improvement in hearing for the entire Series I amounted to 13 dB

In the speech-frequency spectrum, hearing was improved by 10 dB or more in 51 cases, i. e. appx. 63 per cent. In 10 cases, there was a hearing loss of 10 dB or more, i. e. appx. 12 per cent.

The improvement in hearing culminates, as a rule, from one to three months after the operation, after which time hearing losses of 10 dB or more occured in 24 cases (30 per cent).

The following data for each group will be found in Table 3

1. The average improvement in hearing.

2. The number of cases where the post operative threshold of hearing is 20 dB, 30 dB, or better

3. The number of cases where the post operative air-bone gap is 10 dB 15 dB 20 dB, or less.

The arithmetic mean average improvement in hearing in Group No. 3 is only eight dB when Case 7 (where the normal ossicular system was re-established) is not included. Such a re-establishment of a normally-functioning ossicular system must be considered to be an extreme rarity

The values given in parentheses in the column of mean average improvement of hearing provide the mean value of the maximum improvement measured during the observation period, which is from one month to six years after the operation.

The number of cases observed for six months, one year two years, or longer can be ascertained by consulting the diagrams.

A comparison of the results obtained through reconstruction of the transmission mechanism using bone fragments, remains of ossicles, or polyethylene tube will be found in Table 4

It may readily be seen that polyethylene tube

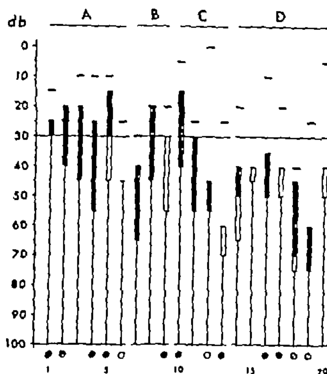


Diagram No 4 Series I Group 4

A. Nos. 1– 6. Interposition of the incus between the stapes footplate and the tympanic membrane.
B. Nos. 7– 9 Interposition of the head of the malleus between the stapes footplate and the tympanic membrane (in Cases 8 and 9 supplemented by a little piece of bone)
C. Nos. 10–13 Interposition of a bone fragment between the stapes footplate and the tympanic membrane
D Nos. 14–20 Interposition of a polyethylene tube between the stapes footplate and the tympanic membrane

made to improve the position of the interposed pieces of bone, but the patient's hearing subsequently deteriorated again

In six cases where the lenticular process or the long process is missing the incus has been interposed between the footplate and the tympanic membrane (with the short process or the long process resting on the footplate and with the body of the incus contacting the tympanic membrane) No special effort has been made to secure contact with the handle of the malleus, or to place the body of the incus under the handle of the malleus.

Cases 5 and 6 are the second and the third re-operation of Case 7 in Group No 1 The original operation and first re-operation have already been discussed. During the second and third re-operations, the stapedial arch was found to be completely necrotized, which is the reason for their inclusion in Group No 4 Under the second re-operation, the incus was interposed between the footplate and the tympanic membrane. There was an immedia improvement in hearing (15 dB) but after period of three years, the final result was 15 dB loss of hearing The third re-operatic disclosed that the incus was fixed to the re wall by a fibrous band, but loosening of th band produced no improvement in hearin function.

The patient listed as Case 18 has been re operated twice. A polyethylene tube was in troduced between the footplate and the tym panic membrane during the original operation It was discovered during the first re-operatio (Case 19) that the polyethylene prosthesis ha disappeared (perforated through the tympani membrane?) Another polyethylene tube wa therefore introduced, bridging from the foot plate to the tympanic membrane. During th second re-operation (Case 13) the polyethylene tube was found to be somewhat dislocated An effort was then made to introduce a piece of bone between the footplate and the tympanic membrane but the footplate was injured during this operation, resulting in a 10 dB loss of hearing.

Case 20 likewise represents a re-operated patient During the original operation, a polyethylene tube was interposed between the foot plate and the tympanic membrane The patient was thereafter periodically disturbed by attacks of a feeling of instability especially when changing the attitude of the head, and a slight hearing loss of 10 dB developed Re-operation disclosed that the polyethylene tube had caused a perforation of the footplate The oval window was then covered with a piece of vein, and the polyethylene tube interposed between the bit of vein and the tympanic membrane This re-operation is not included in Series I

The results of this group are tabulated in Diagram No 4

Table 3

	Quantity	Arithmetic mean increase in hearing	Number of cases at or above specified level		Post-operative air-bone gap		
		dB	20 dB level	30 dB level	10 dB or less	15 dB	20 dB
Group No. 1 Defective lenticular process, luxation of the incudo-stapedial joint	9	5 (12)	1	6	2	3	3
Group No. 2 Partial or complete absence of the incus, luxation of the incus	44	18 (22)	15	30	18	27	35
Interposition of the incus between the head of the stapes and the tympanic membrane	30	13 (19)	8	18	12	18	23
Group No. 3 Necrosis or fracture of the stapedial arch	8	14 (24)	3	6	3	6	6
Group No. 4 Partial or complete absence of the incus combined with defective stapedial arch	20	4 (11)	1	6	5	7	8

The mean improvement in hearing for the entire Series I amounted to 13 dB.

In the speech-frequency spectrum, hearing was improved by 10 dB or more in 51 cases, i.e. appx. 63 per cent. In 10 cases, there was a hearing loss of 10 dB or more, i.e. appx. 12 per cent.

The improvement in hearing culminates as a rule, from one to three months after the operation, after which time hearing losses of 10 dB or more occured in 24 cases (30 per cent).

The following data for each group will be found in Table 3

1 The average improvement in hearing.

2. The number of cases where the post operative threshold of hearing is 20 dB 30 dB, or better

3 The number of cases where the post operative air-bone gap is 10 dB, 15 dB, 20 dB, or less.

The arithmetic mean average improvement in hearing in Group No. 3 is only eight dB when Case 7 (where the normal ossicular system was re-established) is not included. Such a re-establishment of a normally-functioning ossicular system must be considered to be an extreme rarity

The values given in parentheses in the column of mean average improvement of hearing provide the mean value of the maximum improvement measured during the observation period, which is from one month to six years after the operation.

The number of cases observed for six months, one year two years, or longer can be ascertained by consulting the diagrams.

A comparison of the results obtained through reconstruction of the transmission mechanism using bone fragments, remains of ossicles, or polyethylene tube will be found in Table 4

It may readily be seen that polyethylene tube

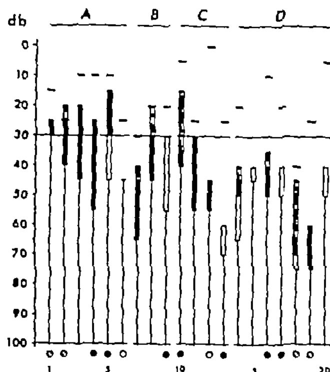


Diagram No. 4 Series I Group 4

A. Nos. 1–6. Interposition of the incus between the stapes footplate and the tympanic membrane

B Nos. 7–9 Interposition of the head of the malleus between the stapes footplate and the tympanic membrane (In Cases 8 and 9 supplemented by a little piece of bone).

C. Nos. 10–13 Interposition of a bone fragment between the stapes footplate and the tympanic membrane

D Nos. 14–20. Interposition of a polyethylene tube between the stapes footplate and the tympanic membrane

made to improve the position of the interposed pieces of bone, but the patient's hearing subsequently deteriorated again.

In six cases where the lenticular process or the long process is missing, the incus has been interposed between the footplate and the tympanic membrane (with the short process or the long process resting on the footplate, and with the body of the incus contacting the tympanic membrane) No special effort has been made to secure contact with the handle of the malleus, or to place the body of the incus under the handle of the malleus.

Cases 5 and 6 are the second and the third re-operation of Case 7 in Group No 1 The original operation and first re-operation have already been discussed During the second and third re-operations, the stapedial arch was found to be completely necrotized, which is the reason for their inclusion in Group No. 4 Under the second re-operation, the incus was interposed between the footplate and the tympanic membrane There was an immediate improvement in hearing (15 dB) but after a period of three years, the final result was a 15 dB loss of hearing The third re-operation disclosed that the incus was fixed to the rear wall by a fibrous band, but loosening of this band produced no improvement in hearing function

The patient listed as Case 18 has been re operated twice. A polyethylene tube was introduced between the footplate and the tympanic membrane during the original operation. It was discovered during the first re-operation (Case 19) that the polyethylene prosthesis had disappeared (perforated through the tympanic membrane?) Another polyethylene tube was therefore introduced bridging from the foot plate to the tympanic membrane During the second re-operation (Case 13) the polyethylene tube was found to be somewhat dislocated. An effort was then made to introduce a piece of bone between the footplate and the tympanic membrane but the footplate was injured during this operation, resulting in a 10 dB loss of hearing

Case 20 likewise represents a re-operated patient. During the original operation, a polyethylene tube was interposed between the foot plate and the tympanic membrane The patient was thereafter periodically disturbed by attacks of a feeling of instability especially when changing the attitude of the head and a slight hearing loss of 10 dB developed Re-operation disclosed that the polyethylene tube had caused a perforation of the footplate. The oval window was then covered with a piece of vein, and the polyethylene tube interposed between the bit of vein and the tympanic membrane. This re-operation is not included in Series I

The results of this group are tabulated in Diagram No. 4

CLINICAL REPORT II

As the reader will have noted from the contents of the concluding paragraphs of the preceeding material, the results of ossicular plastic surgery are not completely satisfactory

In order to examine some of the purely mechanial aspects of the deciding factors in making successful reconstructions of defective ossicular systems, B. S. Elpern (1965 1966, 1966) and the author have performed a series of sound-transmission experiments on dissected temporal bones, where reconstructive surgery on the auditory ossicles was simulated. Among the relationships revealed were: 1 Optimal transmission of sound occured with the use of a prosthesis which fitted precisely so as to make good and stable contact with the remainder of the ossicular system, 2. Connection of the prosthesis to the handle of the malleus provided better conduction of the high frequencies, 3 Even though the head of the malleus was missing, a prosthetic connection of the handle of the malleus to the stapes provided optimal transmission of sound in the frequency spectrum used during these experiments, i. e. up to 4000 Hz, 4 Increased tension in the transmission system (I. e. those changes brought about by certain displacements of the ossicles) resulted in low-frequency transmission losses, 5 The distance from the head of the stapes to the handle of the malleus or the tympanic membrane varies considerably from one specimen to another Consequently the body of the incus, which has relatively constant dimensions, is not always suitable for interposition between the stapes head and the handle or the tympanic membrane, if the conditions of Point 1 above are to be met.

It now becomes possible to ask the following question: Is it possible to improve the results of ossicular plastic surgery (as judged by tone audiograms)· firstly when the above-mentioned mechanical principles are observed, and secondly when the clinical experience as expressed in the concluding paragraphs on page 32 is used?

In order to reply to these questions, the author has performed a number of operations on patients with defective ossicular system, where the above mentioned observations have been sought used to best advantage

This patient group consists of 55 persons, three of whom were operated in both ears, so that this second series contains the results of operations on 58 ears, and Series II is thus of the same numerical order as Series I. As was the case in Series I, all of the patients in Series II had intact tympanic membrans, although these were often cicatrized, and the middle ear was air-filled in all cases.

Two patients have been excluded from the series. In both of these cases, large perforations of the tympanic membranes occured post-operatively and these perforations would have significantly influenced the post-operative hearing of the patients. In one of these cases, the cause of perforation was a post-operative infection. The other patient had been radiologically treated for a reticulo-sarcoma in the rhinopharynx, and thereafter developed a loss of hearing because of a radiation-induced defect in the ossicular system (fibrous degeneration of the long process of the incus) Post-operatively a perforation of the entire posterior portion of the pars tensa slowly developed (perhaps due to reduced vitality caused by the radiation?)

Statistical material in Series II has been treated in the same manner as in the preceding Series I.

The patient group is distributed according to age and sex as can be seen in Table 5

Table 4

	Quantity	Arithmetic mean improvement in hearing	Number of cases at or above specified level		Post-operative air-bone gap		
		dB	20 dB level	30 dB level	10 dB	15 dB	20 dB
1 Ossicular Remains	41	13	11	25	18	26	3
2 Bone Fragments	1	16	4	9	4	5	7
3 Polyethylene Tube	25	9	4	11	4	9	10

has produced worse results than either ossicular remains or bone fragments. In a couple of cases (Diagram 2, Cases 32 and 33) good improvements in hearing lasting more than four years have been achieved using bone prostheses

Complications

As previously mentioned in one case re-operation disclosed that the stapes footplate was ulcerated through the agency of the polyethylene tube prosthesis (Diagram 4 Case 20) This caused a slight loss of hearing of about 10 dB (which was measured as a drop in the bone-conduction threshold ranging from five to 20 dB) However a quite distressing dizziness following changes in attitude resulted from this injury

In another case (Diagram 4 Case 18) the stapes footplate was injured during the second re-operation (Case 13) which only resulted in a slight loss of hearing of about 10 dB (measurement of bone-conduction threshold indicated reductions of from 25 to 40 dB) There have been no cases with a total loss of the cochlear function.

Three patients have post-operatively complained of slight disturbances of the taste sense

Infection of the middle ear has been observed post-operatively in two cases, but the infection was quickly cleared up with the use of antibiotica More serious infections, such as labyrinthitis or meningitis, have not been observed nor have there been any cases of facial paralysis.

Conclusions

The relatively limited size of this clinical series, and the resultant uncertainty of the data thus collected must be taken into consideration when attempting to draw conclusions from this material.

Essentially however the results seem to be in agreement with what would be expected after study of the literature

1 Polyethylene tube must be considered to be an unsuitable material for the reconstruction of the sound transmission mechanism in most cases.

2 Pieces of bone and the remains of ossicles are quite suitable, and can produce satisfactory results of longer duration, but in 26 per cent of these cases, the initial improvement in hearing was found to deteriorate by at least 10 dB after an interval of from one to three months.

3 The average improvement in hearing are greatest when the stapes is intact. This, however is not valid for the group with a defective lenticular process of the incus or a luxation of the incudo-stapedial articulation. In these cases, the improvement in hearing is astonishingly poor but it should be noted that this group consists of only nine patients.

4 Even in cases where the stapes is intact the hearing improvements obtained are extremely variable, and do not bear comparison with the results obtained with modern otosclerosis surgery (Andersen and Warrer 1966)

cases replaced by fibrous cords. In the remaining 16 cases, the stapedial arch was also more or less defective.

A case of cholesteatoma behind an intact tympanic membrane was found in this series as well. Like the case in Series I, this patient could not provide any anamnesis of otitis media, paracentesis, etc., for which reason this case must likewise be considered to be a primary cholesteatoma. The operation disclosed that the cholesteatoma had caused the destruction of the long process of the incus, but the head of the malleus was also found to be fixed to the wall of the atticus.

In 11 of the 13 cranial traumatic cases causing loss of hearing, there are reports of bleeding, and in at least two of these cases, leakage of cerebro-spinal fluid was also reported. In one of these later cases, cerebral matter was found in the external meatus. Three patients had experienced temporary facial paralysis. These figures with the corresponding figures in Series I naturally are no indication of the frequency of ossicle luxation in patients having displayed aural haemorrhage after cranial trauma, but they emphasize the importance of examining such patients both otologically and radiologically

In eight cases, the incus was found to be luxated, and in three of these cases, it was luxated completely out of the field of the operation, and could not be found. In two cases, the handle of the malleus was found to be fractured, in addition to the luxation of the incudo-stapedial articulation. In another case a luxation of both incus and malleus was found combined with a fixation of the malleus in the epitympanic recess. In one case, an incus luxation was found combined with a fracture of the stapes crura. In the remaining case, an isolated fracture of the stapes crura was observed.

In eight other cases, the loss of hearing occurred after mastoidectomy In six of these cases, there was no trace of the incus. In one case, the malleus was also missing, but in spite of this, the patient's tympanic membrane was intact. In the last two cases, the incus was found to be rather severely dislocated.

In one case, loss of hearing occured after a trauma caused by a foreign body (a twig) inserted through the external meatus. The operation disclosed a luxation of the incudo-stapedial articulation.

Two cases have been tabulated under the heading Aetiology Unknown In these cases, the hearing loss occurred gradually and the tympanic membranes were normal. The operation disclosed that the long process of the incus was defective in both cases.

As was expected, the features disclosed by surgery in both Series I and Series II indicate that ossicular defects are most often centered on the incus, while the stapedial arch is also frequently defective as well. It is noteworthy that in both series, isolated fracture and luxation of the stapes crura has been observed a total of ten times. It should also be noted that in four cases, a fracture of the handle of the malleus has been confirmed in addition to luxation of the incus. In two cases, a luxation of the malleus has also been observed.

Perusal of Diagrams 1 to 6 suggets that the pre-operative air-bone gap in Series II has varied from 15 to 65 dB It has previously been stated that an ossicular defect with intact tympanic membrane should produce a loss of hearing of approximately 50 to 60 dB (page 1), but that hearing losses of less severity than expected might be due to fibrous cords or bands from the stapes (e. g. from the stapes footplate) to the long process of the incus, the handle of the malleus, or the tympanic membrane.

Series II contained a group of 37 cases where a pre-operative air-bone gap of from 15 to 40 dB was measured, and in 28 of these cases, the above-mentioned fibrous connections were found. However there were nine cases with such fibrous connections among a group of 21 patients whose air-bone gaps were in the range of 40 to 50 dB

These figures do support the assumption, though, that the fibrous bands and cords are

Table 5

Age	Men	Women	Total	Percentage
5–14	4	1	5	9
15–24	8	8	16	29
25–34	6	4	10	18
35–44	5	3	8	15
45–54	5	5	10	18
55–64	4	2	6	11
Total	3	23	55	100

Examinations

The patients have been examined according to the same principles and procedures as for Series I

It should be noted that emphasis has been placed on negative results of Rinne s Tuning fork Test in both Series I and Series II This implies that the ear in question has an air bone gap of at least 15 dB

Impedance tests have been performed in 37 cases in 27 of these the cross-coupling method was used (Neergaard et al. 1965) In five cases, stapedius reflex reactions of various strengths were detected. Operations on these patients revealed fibrous cords or bands from the stapes to the tympanic membrane, the handle of the malleus or the long process of the incus, explaining the impedance changes due to the stapedius reflex. In four ears, stronger tactile tensor reflex reactions than in the corresponding (normal) ear were detected This can be interpreted, as previously mentioned, as the effect of a greater looseness of the malleus, due to the defect in the ossicular system In this series the pressure in the middle ear was also measured in 27 cases (Terkildsen 1962) In 17 cases, the pressure in the middle ear was found to be normal which has been interpreted as indicating that the Eustachian tube functioned normally In three cases, the middle-ear pressure could not be determined. This was found in one case, to be due to a little cholesteatoma behind the tympanic membrane In seven cases, a slightly negative pressure was measured (ranging from – 6 cm to – 12 cm of water) but in spite of this it has been possible

Table 6 *Distribution According to Aetiology*

	Total	Men	Women
Post-infectious	33	15	18
Cholesteatomal	1		1
Post-traumatic	2_	16	6
(cranial)	13	10	3
(operative)	8	5	3
(transmeatal)	1	1	
Unknown	2		
Total	58	33	_5

to achieve satisfactory and apparently lasting improvements in the hearing function. With the exception of the middle-ear pressure measurements, no examinations of function of the Eustachian tube have been made in Series II

Tomographic X-ray examinations in the frontal and sagittal planes have been performed in 50 cases, and in 29 cases there was good agreement between the tomographic and operative observations In Series I the corresponding figures were 41 and 20 which indicates that the tomographic X ray examination with the Polytome has been of greater diagnostic value in Series II than in Series I It should be noted that the tomographic examination seems, to an increasing degree to be able to provide a diagnosis even in cases of less obvious defects in the ossicles, such as a defective long process of the incus.

Surgical Evidence

Five of the 33 patients in the post-infectious group were unable to provide any information about previous occurrence of otitis media or any other reason for their hearing loss. However due to the fact that the tympanic membrane in each case was cicatrized, they have been included in that group In 17 cases, the operation disclosed that the lenticular process and the long process of the incus were defective to a greater or lesser degree, and in some

ses replaced by fibrous cords. In the remaining 16 cases, the stapedial arch was also more or less defective.

A case of cholesteatoma behind an intact tympanic membrane was found in this series as well. Like the case in Series I, this patient could not provide any anamnesis of otitis media, paracentesis, etc., for which reason this case must likewise be considered to be a primary cholesteatoma. The operation disclosed that the cholesteatoma had caused the destruction of the long process of the incus, but the head of the malleus was also found to be fixed to the wall of the atticus.

In 11 of the 13 cranial traumatic cases causing loss of hearing, there are reports of bleeding, and in at least two of these cases, leakage of cerebro-spinal fluid was also reported. In one of these later cases, cerebral matter was found in the external meatus. Three patients had experienced temporary facial paralysis. These figures with the corresponding figures in Series I naturally are no indication of the frequency of ossicle luxation in patients having displayed aural haemorrhage after cranial trauma, but they emphasize the importance of examining such patients both otologically and audiologically

In eight cases, the incus was found to be luxated, and in three of these cases, it was luxated completely out of the field of the operation, and could not be found. In two cases, the handle of the malleus was found to be fractured, in addition to the luxation of the incudo-stapedial articulation. In another case a luxation of both incus and malleus was found combined with a fixation of the malleus in the epitympanic recess. In one case, an incus luxation was found combined with a fracture of the stapes crura. In the remaining case, an isolated fracture of the stapes crura was observed.

In eight other cases, the loss of hearing occurred after mastoidectomy In six of these cases, there was no trace of the incus. In one case, the malleus was also missing, but in spite of this, the patient's tympanic membrane was intact. In the last two cases, the incus was found to be rather severely dislocated.

In one case, loss of hearing occured after a trauma caused by a foreign body (a twig) inserted through the external meatus. The operation disclosed a luxation of the incudo-stapedial articulation.

Two cases have been tabulated under the heading Aetiology Unknown In these cases, the hearing loss occurred gradually and the tympanic membranes were normal. The operation disclosed that the long process of the incus was defective in both cases.

As was expected, the features disclosed by surgery in both Series I and Series II indicate that ossicular defects are most often centered on the incus, while the stapedial arch is also frequently defective as well. It is noteworthy that in both series, isolated fracture and luxation of the stapes crura has been observed a total of ten times. It should also be noted that in four cases, a fracture of the handle of the malleus has been confirmed in addition to luxation of the incus. In two cases, a luxation of the malleus has also been observed.

Perusal of Diagrams 1 to 6 suggests that the pre-operative air-bone gap in Series II has varied from 15 to 65 dB. It has previously been stated that an ossicular defect with intact tympanic membrane should produce a loss of hearing of approximately 50 to 60 dB (page 12) but that hearing losses of less severity than expected might be due to fibrous cords or bands from the stapes (e g. from the stapes footplate) to the long process of the incus, the handle of the malleus, or the tympanic membrane.

Series II contained a group of 37 cases where a pre-operative air-bone gap of from 15 to 40 dB was measured, and in 28 of these cases, the above-mentioned fibrous connections were found. However there were nine cases with such fibrous connections among a group of 21 patients whose air-bone gaps were in the range of 40 to 50 dB

These figures do support the assumption, though, that the fibrous bands and cords are

Table 5

Age	Men	Women	Total	Percentage
5–14	4	1	5	9
15–24	8	8	16	9
25–34	6	4	10	18
35–44	5	3	8	15
45–54	5	5	10	18
55–64	4	2	6	11
Total	32	23	55	100

Table 6 *Distribution According to Aetiology*

	Total	Men	Women
Post infectious	33	15	18
Cholesteatomal	1		1
Post traumatic	22	16	6
(cranial)	13	10	3
(operative)	8	5	3
(transmeatal)	1	1	
Unknown	2	2	
Total	58	33	25

Examinations

The patients have been examined according to the same principles and procedures as for Series I

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Table 6 *Distribution According to Aetiology*

	Total	Men	Women
Post-infectious	33	15	18
Cholesteatomal	1		1
Post traumatic	2[illegible]	16	6
(cranial)	13	10	3
(operative)	8	5	3
(transmeatal)	1	1	
Unknown	2	2	
Total	58	33	[illegible]5

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Surgical Evidence

Five of the 33 patients in the post infectious group were unable to provide any information about previous occurrence of otitis media or any other reason for their hearing loss. However due to the fact that the tympanic membrane in each case was cicatrized, they have been included in that group In 17 cases, the operation disclosed that the lenticular process and the long process of the incus were defective to a greater or lesser degree and in some

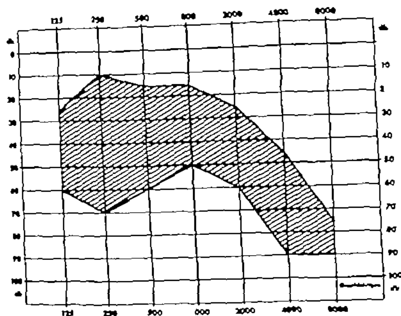


Fig. 2. Hearing improvement obtained three days after the operation (Diagram 5 Case 12).

tion of the handle of the malleus ventrally in the tympanic cavity

It can be seen that the bone prosthesis has excavations which serve to ensure a good and stable contact with the head of the stapes and the handle of the malleus, and in addition, there is a slightly curved surface where the prosthesis will contact the tympanic membrane, which contributes to stability when the tympanic membrane is returned to its correct position at the conclusion of the operation. The thickness of the bone is about 2 mm. In the greatest majority of cases, the bone prosthesis has been cut out of the cortex of the lateral surface of the mastoid process. In three cases only has the body of the incus provided the material for the prosthesis.

Using bone prostheses of the type described, it has occasionally been possible to obtain a convincing improvement in hearing very quickly after the operation, as may be seen by study of Figure 2, which shows the hearing improvement obtained three days after the operation (Diagram 5 Case 12)

Due to the fact that this is too early for fibrous adhesion processes to have taken place, this effect must indicate that the bone prosthesis works satisfactorily in the purely mechanical sense. The installation of these bone prostheses has had the primary aim of creating a columella effect, but it is possible that the handle and the prosthesis develop a certain leverage effect as well.

The results are tabulated in Diagram 5

Cases 26 28 and 33 are re-operations of Cases 25 27 and 32 respectively The re-operations of Cases 26 and 28 disclosed that there was poor contact with the stapes. New prostheses which fitted better were formed, and a good improvement in hearing was achieved in these two cases. Re-operation of Case 33 did not provide any clear explanation of the reason for the lack of improvement in hearing.

After the operation of Case 31 a conductive hearing loss of 30 dB has resulted. Tomography has shown that the bone prosthesis has slipped out of position, but this patient has not yet been re-operated.

In Case 40 both the incus and malleus were missing (after mastoidectomy in childhood), while the stapes was intact and mobile. As can be seen, a bone prosthesis interposed between the stapes and the intact tympanic membrane produced an exceptional improvement in the patient's hearing.

In Case 41 luxations of both the incus and

able to transmit a certain amount of sound through the middle ear But it must be noted that the pre-operative air bone gap in some cases, can apparently be less than expected because of a scarred or perhaps partially atrophied tympanic membrane.

Treatment and Results

Series II as previously mentioned, consists of 58 ears where, due to five re-operations, a total of 63 ossicular plastic operations have been performed A transmeatal approach according to Rosen s method has been used in all of the operations. Nine operations were performed under local anaesthesia, while the remainder were done under a general anaesthesia. It must be considered an advantage to use a local anaesthesia for ossicular plastic surgery as the patient s remarks relating to a subjective improvement in hearing can be a significant aid in correctly positioning the prosthesis.

The character of the ossicular plastic surgery included in this series has depended upon whether or not the stapes has been intact or not. Series II can therefore be divided into two groups:

1 The 42 cases where the stapes was intact

2. The 21 cases where the stapedial arch was absent, while the stapes footplate was normal.

For each operation, as was the case in Series I the following information can be seen in Diagrams 5 and 6.

A. *Hearing improvement* or loss expressed as the arithmetic mean of the speech frequencies 500 1000 and 2000 Hz, measured during the most recent follow-up examination

B The maximum improvement *in the mean* average of the above-mentioned frequencies. This maximum is often observed from one to three months after the operation. By comparing the values of Point A and B the hearing loss occuring during the observation period can be ascertained.

C. Pre-operative bone-conduction as the mean of the speech frequencies 500 1000 and 2000 Hz.

1 *Intact stapes*

This group consists of 42 operations (including two re-operations) In all cases the prosthesis consists of a shaped piece of bone interposed between the head of the stapes and the handle of the malleus and the tympanic membrane. The shape of the bone fragment was determined by the principles which have experimentally displayed (Elbrønd and Elpern, 1966) the optimal sound transmission in the middle ear Consequently the object has been to shape the bone prosthesis so as to fit precisely between the head of the stapes, and the handle of the maleus and the tympanic membrane, ensuring that there is good contact with the stapes head and the handle. In each individual case, the size of the bone fragment is determined by the distance from the stapes head to the handle, measured along a perpendicular to the handle (Fig. 1) It is possible to measure this dimension with relatively great accuracy (0 1 mm) *In this series of operations, this dimension has* varied from about 1 0 mm to approximately 2.2 mm In one case, however the distance was 2.6 mm, but this was due to a slight luxa-

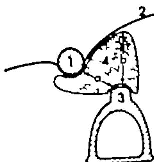


Fig. 1

1 Handle of malleus.
2 Tympanic membrane.
3 Head of stapes.
4 Bone prosthesis.
a. Distance from stapes head to malleus handle
b. Distance from stapes head to tympanic membrane (equals *a* plus 1.3 ± 0.1 mm).

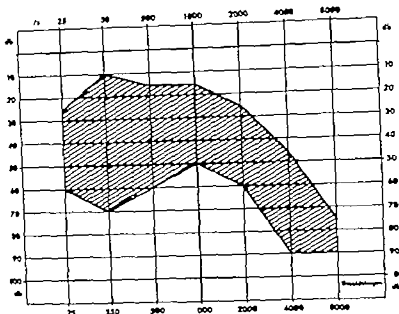


Fig. 2. Hearing improvement obtained three days after the operation (Diagram 5 Case 12).

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It can be seen that the bone prosthesis has excavations which serve to ensure a good and stable contact with the head of the stapes and the handle of the malleus, and in addition, there is a slightly curved surface where the prosthesis will contact the tympanic membrane, which contributes to stability when the tympanic membrane is returned to its correct position at the conclusion of the operation. The thickness of the bone is about 2 mm. In the greatest majority of cases, the bone prosthesis has been cut out of the cortex of the lateral surface of the mastoid process. In three cases only has the body of the incus provided the material for the prosthesis.

Using bone prostheses of the type described, it has occasionally been possible to obtain a convincing improvement in hearing very quickly after the operation, as may be seen by study of Figure 2, which shows the hearing improvement obtained three days after the operation (Diagram 5 Case 12).

Due to the fact that this is too early for fibrous adhesion processes to have taken place, this effect must indicate that the bone prosthesis works satisfactorily in the purely mechanical sense. The installation of these bone prostheses has had the primary aim of creating a columella effect, but it is possible that the handle and the prosthesis develop a certain leverage effect as well.

The results are tabulated in Diagram 5.

Cases 26, 28, and 33 are re-operations of Cases 25, 27 and 32 respectively. The re-operations of Cases 26 and 28 disclosed that there was poor contact with the stapes. New prostheses which fitted better were formed, and a good improvement in hearing was achieved in these two cases. Re-operation of Case 33 did not provide any clear explanation of the reason for the lack of improvement in hearing.

After the operation of Case 31 a conductive hearing loss of 30 dB has resulted. Tomography has shown that the bone prosthesis has slipped out of position, but this patient has not yet been re-operated.

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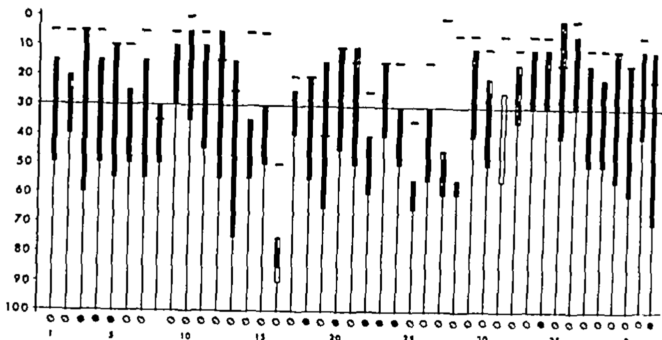


Diagram No. 5 Series II Group 1

Nos. 1–4... Interposition of a shaped piece of bone between the head of the stapes, the handle of the malleus and the tympanic membrane.

the malleus were found, as the result of a cranial trauma. The stapes was intact and mobile The head of the malleus was found to be tightly wedged in the anterior part of the attic, for which reason the neck of the malleus was severed The handle of the malleus was then free to move and the head of the malleus and the incus were removed

A little cholesteatoma was disclosed in Case 42 and it was found to have caused the de struction of the distal part of the long process of the incus. In addition the head of the mal leus was fixed in the attic, while the stapes was intact and mobile. As in the preceding case, the neck of the malleus was severed so that the head of the malleus and the incus could then be extracted In both Cases 41 and 42, shaped pieces of bone were interposed between the stapes and the handle and the tympanic membrane Good improvement in hearing is seen to have been obtained in both cases, in spite of the lack of the head of the malleus, which is in agreement with the results of ex perimental research (Elpern and Elbrønd 1966)

2 *Defective stapedial arch*

This group consists of 21 operations (including two re-operations) In 13 operations, the incus has been interposed between the stapes foot plate and the handle of the malleus. As it was reported on page 20 the distance from the footplate to the handle corresponds quite precisely in many cases to the distance from the apex of the short process of the incus to the middle of the saddle shaped articular surface on the body of the incus. The incus has consequently been interposed in these cases, with the handle resting in the middle of the saddle-shaped articulation surface The re mainder of the long process of the incus was first excised, to prevent interference with the promontory Experimentally the interposition of the incus in this manner has produced opti mal transmission of sound in temporal-bone preparations (Elbrønd and Elpern, 1966)

In two cases (Cases 10 and 12 in Diagram 6) the short process of the incus was found to be too long, and a bit of the apex of the short process was then removed. It then became

possible to place the incus in position between the footplate and the handle. Elsewhere, in Case 2, the incus was found to be a bit too short, and consequently a little piece of cartilage (from the tragus) was placed between the articulation surface on the body of the incus and the handle, in order to provide sufficient contact.

In Case 14 where the incus was found to be partially destroyed, a shaped piece of bone was interposed between the stapes footplate and the handle and the tympanic membrane. This bone prosthesis was provided with a depression, excavated as in the bone prostheses of the preceding group, fitting the manubrium and having a curved contact surface facing the tympanic membrane, and with a projection resting on the footplate.

Teflon prostheses shaped to fit each individual application were used in six cases, as this procedure had also been experimentally shown to give optimal sound transmission when tested in temporal-bone preparations (Elbrønd and Elpern, 1966) interposed between the footplate and the malleus, with a clasp fitting around the handle of the malleus.

Case 20 is a re-operation of Case 19. During the first operation, a teflon prosthesis was interposed between the stapes footplate and the handle of the malleus. This resulted in an exceptional improvement in hearing, but after approximately one month, a sudden loss of hearing occurred when the patient was subjected to a sudden change in pressure (slamming of a car door). Re-operation disclosed that the prosthesis had slipped rearward on the footplate so that there was very poor contact. The prosthesis was again placed in contact with the footplate, all the way foreward by the stump of the anterior crus. Again an exceptional improvement in hearing was achieved, lasting for about four weeks. The second re-operation (Case 3) did not reveal the presence of the teflon prosthesis anywhere in the tympanic cavity. The handle was found to be defective, for which reason it has been assumed that the prosthesis has been rejected through

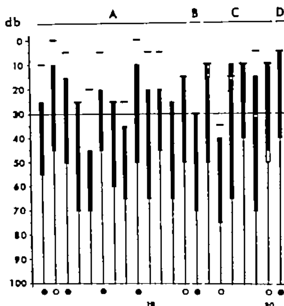


Diagram No. 6. Series II, Group 2.

A. Nos. 1-13.	Interposition of the incus between the stapes footplate and the handle of the malleus.
B. No. 14	Interposition of bone fragment between the stapes footplate, the handle of the malleus and the tympanic membrane.
C. Nos. 15–20.	Interposition of teflon prosthesis between the stapes footplate and the handle of the malleus.
D. No. 21	Interposition of bone fragment between the stapes footplate and the long process of the incus.

the handle and tympanic membrane. During this operation, the remains of the incus were located in the attic, and it was then interposed in the previously-described manner between the stapes footplate and the handle of the malleus.

In reconstruction of the sound-transmission mechanism during the operations discussed in the paragraphs above, a columella effect has been sought, but it is not impossible that there also is a certain leverage effect developed by the handle of the malleus and the incus prosthesis.

A fracture of the stapes crura was found in Case 21 while the remainder of the ossicular system was found to be normal. In this case, a carefully-dimensioned piece of bone was in-

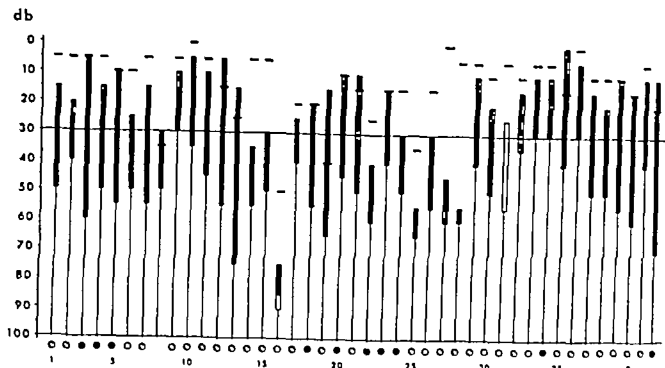


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A little cholesteatoma was disclosed in Case 42, and it was found to have caused the de struction of the distal part of the long process of the incus. In addition the head of the mal leus was fixed in the attic, while the stapes was intact and mobile. As in the preceding case the neck of the malleus was severed so that the head of the malleus and the incus could then be extracted In both Cases 41 and 42, shaped pieces of bone were interposed between the stapes and the handle and the tympanic membrane. Good improvement in hearing is seen to have been obtained in both cases, in spite of the lack of the head of the malleus, which is in agreement with the results of ex perimental research (Elpern and Elbrønd, 1966)

2. *Defective stapedial arch*

This group consists of 21 operations (including two re-operations) In 13 operations, the incus has been interposed between the stapes foot plate and the handle of the malleus. As it was reported on page 20 the distance from the footplate to the handle corresponds quite precisely in many cases to the distance from the apex of the short process of the incus to the middle of the saddle-shaped articular surface on the body of the incus The incus has consequently been interposed in these cases, with the handle resting in the middle of the saddle-shaped articulation surface. The re mainder of the long process of the incus was first excised, to prevent interference with the promontory Experimentally the interposition of the incus in this manner has produced opti mal transmission of sound in temporal bone preparations (Elbrønd and Elpern 1966)

In two cases (Cases 10 and 12 in Diagram 6) the short process of the incus was found to be too long, and a bit of the apex of the short process was then removed. It then became

DISCUSSION

The following question has previously been stated in the beginning of the preceding section: "It is possible, on the basis of the previously-described clinical and experimental evidence and conclusions, using tone audiograms as the criteria, to improve the results of reconstructive surgery on defective ossicular systems?"

The basis for an answer to this question must lie in a comparison between the improvement in hearing achieved in Series I and Series II.

This sort of comparison can be made between each group and series, using the mean average improvement (or loss) of the hearing function at the frequencies 500 1000 and 2000 Hz. The following results can then be tabulated.

1 The average improvement in hearing within an entire series or group

2. The number of cases where a threshold of hearing of 30 dB (or perhaps 20 dB) or better has been achieved,

3 The number of cases where a post-operative air-bone gap of 10 dB (or perhaps 15 or 20 dB) or less has been obtained.

The above-specified data can be seen in the tables on pages 31 and 40 Comparison of the results are clearly to the advantage of Series II.

However tabulations of the mean average improvements in hearing, or the losses, at three frequencies, can only provide limited information on the configuration of the pre-operative and post-operative audiogram.

In addition, special non-parametric statistical methods must be used if a comparison is to be made of the results of several series of operations to improve hearing, and the above mentioned average values are to be used as a basis of comparison.

Results of individual operations to improve hearing are best presented by pre-operative and post-operative audiograms. As Wullstein (1967) suggests, it is consequently natural to compute a pre-operative and a post-operative mean-value audiogram when evaluating the improvements achieved in a series of operations aimed at improving hearing. With such mean-value audiograms, the average improvement (or loss) at each individual frequency may be read directly from the graph.

Mean-value audiograms have been prepared as follows.

1 The entire Series I and Series II.

In order to permit the comparison of groups within each series:

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Series II, Group 1 (intact stapes)

The following comparison is of special interest:

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Within each of these two latter groups, the same technique, i.e. interposition of the incus between the stapes and the tympanic membrane has been used throughout Group 2 of Series I, while a shaped piece of bone has been interposed between the stapes, the tympanic membrane, and the handle of the malleus throughout Group 1 of Series II.

Finally the following comparison may be found interesting:

4 Series I, Group 4 and
Series II, Group 2 (defective stapedial arch)

Table 7

	Total	Average hearing improvement	Number of cases at or above specified level		Post-operative air-bone gap		
		dB	20 dB level	30 dB level	10 dB or less	15 dB	0 dB
1 Stapes intact	42	25 (29)	23	32	23	31	35
2. Stapes defective	21	29 (36)	9	14	11	16	16

terposed between the long process of the incus and the footplate It was thus possible to restore the normal function of the ossicular system. Consequently this case does not fit in with the remainder of Group 2, neither in respect to surgical technique nor function

The resulting improvements in hearing are tabulated in Diagram 6

In Table 7 the following results for each group can be read.

1 The mean average improvement in hearing

2. The number of cases where the post operative threshold of hearing is 20 dB 30 dB or better

3 The number of cases where the post operative air-bone gap is 10 dB 15 dB or 20 dB or less

The figures in parentheses indicate the *maximum improvement occuring during the* observation period, which is from one month to three years. A total of 11 cases have been observed for six months, 35 were observed for one year and 14 were observed for two years or more

In Series II as a whole the mean average hearing improvement was 27 dB (Series I 13 dB) A hearing improvement of 10 dB or more was achieved in 54 cases, i. e in approximately *86 per cent* (Series I 63 per cent) In one case a hearing loss exceeding 10 dB occurred, i. e. appx. 1 6 per cent (Series I 12 per cent) After the hearing improvement had culminated which occurs as a rule from one to three months after the operation, 15 cases (or 24 per cent) were observed to have a hearing loss of 10 dB or more (Series I 30 per cent)

Complications

As previously mentioned, there was one case with a post-operative loss of hearing of 30 dB but this was not of the cochlear type. Vestibular disturbances have not been observed

Conclusions

The analysis of Series II indicates that.

1 Pieces of bone and the remains of ossicles as used in 57 operations, can permit reconstruction of the ossicular system so as to produce hearing improvements of longer duration, but in a portion of the cases (at least one fourth) the initial improvement in hearing must be *expected to deteriorate by more* than 10 dB after from one to three months

2. Good improvement in hearing can be obtained in spite of the lack of the head of the malleus.

3 The use of teflon prostheses initially provides an exceptional improvement in hearing, but it seems more difficult to obtain stable results with this material

4 Good improvements in hearing have been obtained in Series II either where the stapes was intact or defective.

5 *The results obtained now* seem to be comparable *with those obtained with otosclerosis* surgery (Andersen and Warrer 1966)

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Finally the following comparison may be found interesting:

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Series II, Group 2 (defective stapedial arch)

Table 7

	Total	Average hearing improvement	Number of cases at or above specified level		Post-operative air-bone gap		
		dB	20 dB level	30 dB level	10 dB or less	15 dB	20 dB
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2 *Stapes defective*	1	29 (36)	9	14	11	16	16

terposed between the long process of the incus and the footplate. It was thus possible to restore the normal function of the ossicular system Consequently this case does not fit in with the remainder of Group 2, neither in respect to surgical technique nor function.

The resulting improvements in hearing are *tabulated in Diagram 6*

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Conclusions

The analysis of Series II indicates that

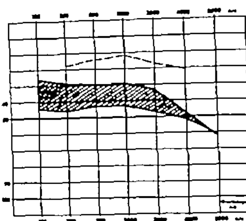
1 Pieces of bone and the remains of ossicles, as used in 57 operations, can permit reconstruction of the ossicular system so as to produce hearing improvements of longer duration, but in a portion of the cases (at least one *fourth) the initial improvement in hearing must* be expected to deteriorate by more than 10 dB after from one to three months.

2 Good improvement in hearing can be obtained in spite of the lack of the head of the malleus.

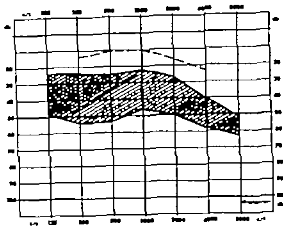
3 The use of teflon prostheses initially provides an exceptional improvement *in hearing,* but it seems more difficult to obtain stable results with this material.

4 Good improvements in hearing have been obtained in Series II either where the stapes was intact or defective.

5 The results obtained now seem to be comparable with *those obtained with otosclerosis* surgery (Andersen and Warrer 1966)



Series I, Group 2 (30 operations).



Series II, Group 1

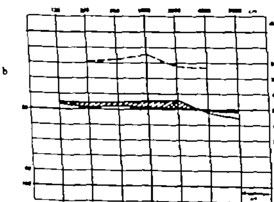
Fig. 5 Mean-value audiograms.
c. Pre-operative bone conduction.
b. Post-operative air conduction.
a. Pre-operative air conduction

by the means and the standard deviations of the means.

The data obtained in Series I and Series II therefore have been considered to be normally distributed.

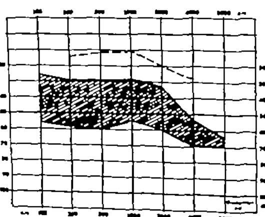
Statistical analysis (the t-test) indicates that—at a probability level of five per cent—a significant improvement in hearing has been obtained for at least five of seven frequencies in Series I and Series II and in the subsidiary groups with the exception of Group 4 of Series I.

Statistical comparison of Series I with Series II, and comparison of the corresponding sub-

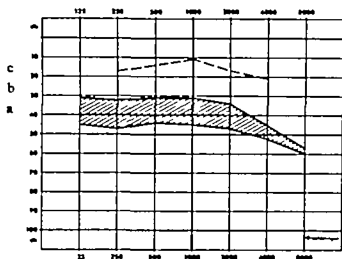


Series I, Group 4.

Fig. 6 Mean-value audiograms.
c. Pre-operative bone conduction.
b. Post-operative air conduction.
a. Pre-operative air conduction.



Series II, Group 2.



Series I

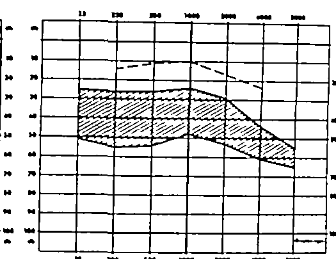
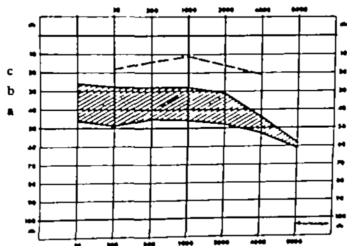

Series II

Fig. 3 Mean value audiograms.
c. Pre-operative bone conduction.
b Post-operative air conduction.
a. Pre-operative air conduction.

Perusal of these audiograms seems to indicate the following

The mean improvement in hearing at each frequency is greater throughout Series II than in Series I This is also seen to be valid for a comparison of the subsidiary groups. In particular the hearing improvement in Group 2 of Series II is significantly greater than for the whole of Group 4 Series I

On the basis of an analysis of a larger number of operations aimed at improving hearing, Wullstein (1967) reports that the data measured can be considered to be normally distributed and for that reason characterized



Series I Group 2 (44 operations).

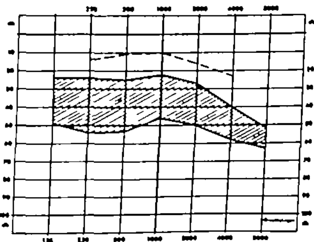
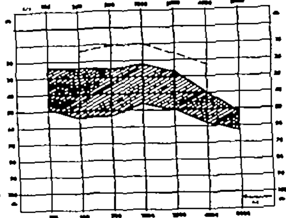

Series II, Group 1

Fig. 4 Mean value audiograms.
c. Pre-operative bone conduction.
b. Post-operative air conduction.
a. Pre-operative air conduction.



Series I, Group 2 (30 operations).



Series II, Group 1

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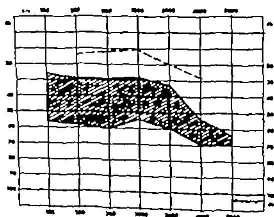
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Statistical analysis (the t-test) indicates that—at a probability level of five per cent—a significant improvement in hearing has been obtained for at least five of seven frequencies in Series I and Series II and in the subsidiary groups with the exception of Group 4 of Series I.

Statistical comparison of Series I with Series II, and comparison of the corresponding sub-



Series I, Group 4.



Series II, Group 2.

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c. Pre-operative bone conduction.
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sidiary groups indicates—with a five per cent probability level—that a significantly greater improvement in hearing has been obtained in Series II when compared with Series I and likewise in comparison of Group 1 of Series II with Group 2 of Series I (30 operations) and Group 2 of Series II with Group 4 of Series I On the other hand, there is no significant difference between Group 1 of Series II and group 2 of Series 1 (44 operations)

However is such a comparison of Series I with Series II and b tween the subsidiary groups at all permissab.e?

It is naturally of deciding importance that Series I and Series II are comparable i e that the sole variable factor involved is the type of reconstructive surgery performed on the sound conduction mechanism

It can hardly be stated that this is the case with any great degree of certainty As it may be seen in the tables on pages 24 25 and 34 the distribution according to age and aetiology is not the same in both series. To this inconsistency must be added unavoidable variation in the observation periods, and that local anaesthesia was used more frequently in Series I than in Series II It is difficult to judge whether or not these conditions have had any real influence to the advantage of one series or the other but it should be noted that in reality Series I and Series II constitute a consecutive series, and that the selection of patients and the surgical indications seem to have been the same in both series.

But there is a difference between the two series which is of deciding importance and that difference, which may be discerned in the middle value audiograms, is that the pre-operative air bone gap is greater in Series II than in Series I There is no sure explanation for this difference A greater pre-operative air bone gap provides the possibility for a greater improvement in hearing, which is seen to be indicated by a regression-correlation analysis to be described below

The above-mentioned statistical analysis which indicated that greater improvement in hearing was obtained in Series II and the subsidiary groups than in Series I and its subsidiary groups (with the exception of Group 1 of Series II 44 operations) thus seems hardly relevant, as it has been made on the basis of the absolute improvement in hearing, without regard for the pre-operative air-bone gap

It is clear that a comparison between the hearing improvements in the two series and their subsidiary groupings must be made on the basis of the relative hearing improvements, i. e the hearing improvement in respect to the pre-operative air bone gap

In Table 8 the percentage of the "closure" of the air-bone gap in each series and the respective subsidiary groups is listed and the calculated differences recorded.

It can be seen that the percentage closure of the air-bone gap is greater in Series II than in Series I This is especially true for a comparison of Group 4 of Series I with Group ? of Series II

Furthermore it is seen that the greatest percentage of closure of the air-bone gap in both series occurs at 250 Hz, and the least at 4000 Hz.

In the third part of the table above, the interposed incus cases in Group 2 of Series I are compared with Group 1 of Series II It may be recalled that in these cases, the incus was interposed between the stapes and the tympanic membrane, without special effort to achieve contact with the handle of the malleus. In Group 1 of Series II precisely-dimensioned pieces of bone were placed between the handle of the malleus, the tympanic membrane and the stapes, a small groove being provided in the bone fragment to fit the handle of the malleus. At all of the frequencies measured the percentage closure of the air bone gap was found to be greater in Group 1 of Series II but it is relatively best at 4000 Hz, where the difference amounts to 38 per cent, while the percentage closure ranges from 14 to 22 per cent for the other frequencies. This can presumably be taken as an indication that the experimentally-demonstrated improvement in the

Table 8. *Percentage Closure of the Air Bone Gap*

Frequency (Hz)	Series I per cent	Series II per cent	Difference between I and II per cent
250	50	71	21
500	43	65	22
1000	41	63	22
2000	45	67	22
4000	23	46	23

	Series I *Group 2*	Series II, Group 1 *(42 operations)*	Difference
250	68	75	7
500	55	67	12
1000	51	67	16
2000	53	68	15
4000	28	51	23

	Series I, Group 2 (interposed incus, 30 operations)	Series II, Group 1 (42 operations)	Difference
250	61	75	14
500	45	67	22
1000	45	67	22
2000	47	68	21
4000	13	51	38

	Series I, Group 4	Series II, Group 2	Difference
250	10	66	56
500	7	65	58
1000	14	60	46
2000	22	69	47
4000	−3	37	40

transmission of the higher frequencies by providing a solid contact between the prosthesis and the handle of the malleus also holds true in vivo (see page 33)

Upon comparing Group 4 of Series I with Group 2 of Series II a similar relatively-greater closure of the air-bone gap at 4000 Hz is not demonstrated in Group 2 of Series II. This may be due to the fact that the arch of the stapes is lacking in these cases, which makes difficult the establishment of a sure and really stable contact between the prosthesis and the footplate of the stapes. An unstable or loose contact will lead to losses in the upper end of the spectrum, which result was predicted by the experimental results obtained with temporal bone preparations.

But, are the relatively greater improvements in hearing in Series II and its subsidiary groups statistically significant? In order to cast light on this problem, regression and correlation analysis has been carried out on this material. Using regression and correlation analysis the functional relationship between the pre-opera-

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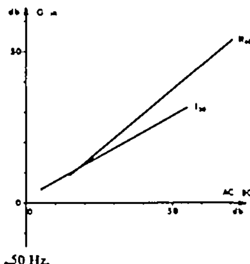
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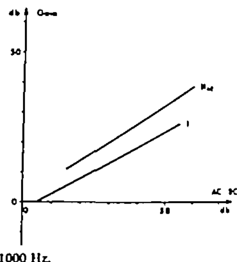
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But, are the relatively greater improvements in hearing in Series II and its subsidiary groups statistically significant? In order to cast light on this problem, regression and correlation analysis has been carried out on this material. Using regression and correlation analysis the functional relationship between the pre-opera-



250 Hz.

Fig. 7 Regression lines for Series I Group (30 operations) and Series II Group 1 (4 operations)



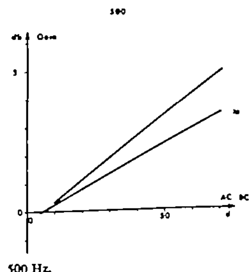
1000 Hz.

Fig. 9 Regression lines for Series I, Group (30 operations) and Series II Group 1 (42 operations).

tive air bone gap and the improvement in hearing obtained can be determined

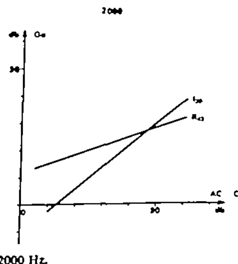
These analyses indicate that there is statistically sure connection between the pre-operative air bone gap and the hearing improvement obtained, as the regression coefficients for each frequency are significantly different from zero (with a five per cent level of probability) in both series and in the subsidiary groups, with the exceptions of Group 4 of Series I and Group 2 of Series II The correlation analysis is in agreement with these results.

In Figures 7 8 9 10 and 11 regression lines for Group 2 of Series I (30 operations) and for Group 1 of Series II have been plotted for the frequencies of 250–4000 Hz in a co-ordinate system having the pre-operative air bone gap as the abscissa, and the hearing improvement obtained as the ordinate. It can be seen that the hearing improvements obtained in Group 1 of Series II seem to have been relatively better—except at 2000 Hz—when the air-bone gap has been of a certain degree of magnitude An analysis indicates, however



500 Hz.

Fig. 8 Regression lines for Series I Group 2 (30 operations) and Series II Group 1 (42 operations).



2000 Hz.

Fig. 10. Regression lines for Series I Group (30 operations) and Series II, Group 1 (4 operations

that no significant difference between any of the corresponding regression coefficients can be demonstrated. This is also true for a comparison of the whole of Series I with the whole of Series II and for a comparison of Group 2 of Series I with Group 1 of Series II.

In Fig. 11 the values of the variables used for the regression calculations for each grouping at the frequency of 4000 Hz have been plotted. It can be seen that the two series over lap one another considerably which is in agreement with the statement that there is no statistically significant difference between the regression coefficients.

The reply to the question stated above (page 33) must thus be that only in Group 2 of Series II has it been possible to prove reliably that greater hearing improvements have been obtained than in the corresponding group in Series I. In Group 1 of Series II, it has not been possible to obtain a statistically significant greater improvement in hearing than in Group 2 of Series I.

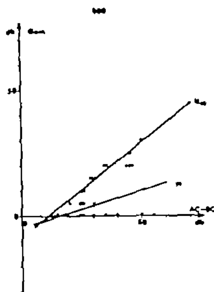
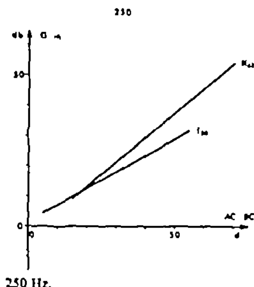
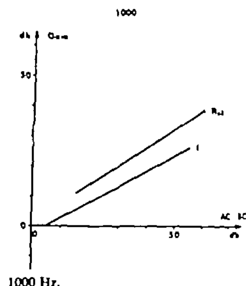


Fig. 11 Regression lines for Series I, Group 2 (30 operations) and Series II, Group 1 (42 operations). The values of the variables used for the calculation of the regressions lines for each grouping have been plotted.



250 Hz.

Fig. 7 Regression lines for Series I Group (30 operations) and Series II Group 1 (42 operations).



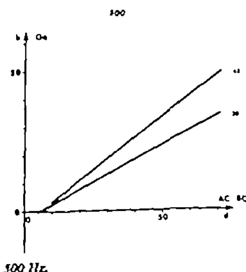
1000 Hz.

Fig. 9 Regression lines for Series I, Group (30 operations) and Series II, Group 1 (4 operations).

tive air bone gap and the improvement in hearing obtained can be determined

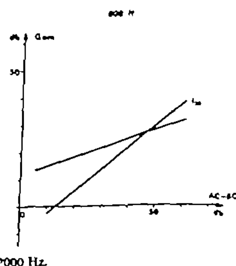
These analyses indicate that there is statistically sure connection between the pre-operative air bone gap and the hearing improvement obtained, as the regression coefficients for each frequency are significantly different from zero (with a five per cent level of probability) in both series and in the subsidiary groups, with the exceptions of Group 4 of Series I and Group 2 of Series II The correlation analysis is in agreement with these results.

In Figures 7 8 9 10 and 11 regression lines for Group 2 of Series I (30 operations) and for Group 1 of Series II have been plotted for the frequencies of 250–4000 Hz in a co-ordinate system having the pre-operative air bone gap as the abscissa, and the hearing improvement obtained as the ordinate It can be seen that the hearing improvements obtained in Group 1 of Series II seem to have been relatively better—except at 2000 Hz—when the air bone gap has been of a certain degree of magnitude An analysis indicates, however



500 Hz.

Fig. 8 Regression lines for Series I Group (30 operations) and Series II Group 1 (42 operations).



2000 Hz.

Fig. 10. Regression lines for Series I Group 2 (30 operations) and Series II Group 1 (4 operations)

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OTO LARYNGOLOGICA

SUPPLEMENTUM 263

Transactions of the XVIIth Congress of the Scandinavian Oto-Laryngological Society

HELSINGØR, DENMARK, JUNE 27–30, 1969

EDITORS

OTTO JEPSEN AND OLE ELBRØND

THE ALMQVIST & WIKSELL PERIODICAL COMPANY

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The manuscripts have been critically revised by

A. Rousing, M T F Århus

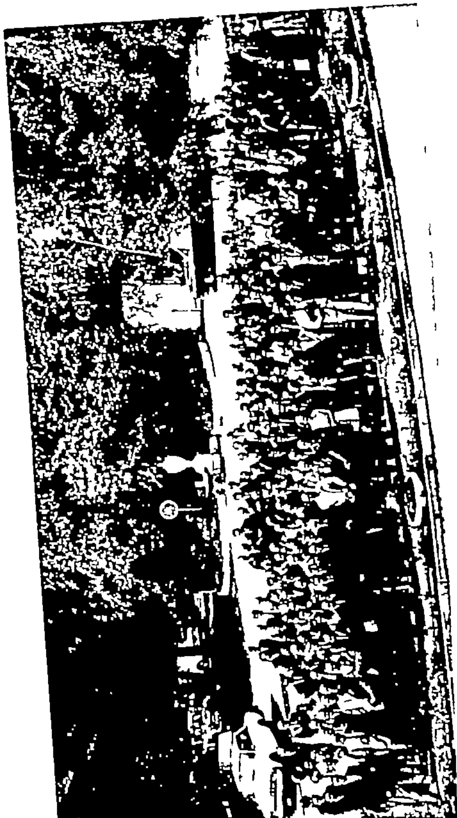
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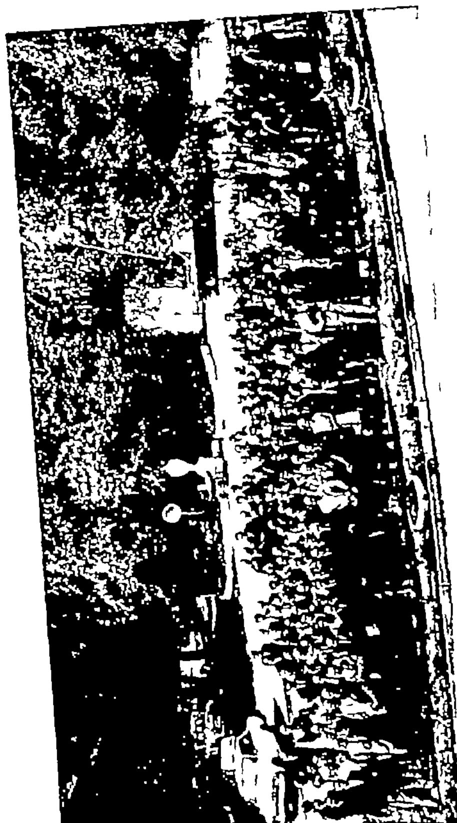
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THE XVIIITH CONGRESS OF THE SCANDINAVIAN OTO-LARYNGOLOGICAL SOCIETY

Helsingør Denmark, June 27–30 1969

The Congress was held at Marienlyst, Helsingør The Congress Committee consisted of Professor *H C Andersen*, President, Professor *H K. Kristensen*, Vice-president; Dr *O Bentzen* Secretary Dr *H Sørensen* Cashier Professor *O Jepsen*, Editor and Dr *O Elbrønd* Assistant Editor The discussion was limited to the following topics.

Function of the Eustachian Tube
Disorders of the Salivary Glands
Phoniatry
Objective Methods of Assessing the Hearing Ability
In addition, a *Scientific Exhibition* was held.

The Congress was attended by 230 active (Denmark 76 Finland, 30 Iceland, 2 Norway 49 Sweden, 78) and 162 passive members.

At the Official Opening, the President addressed the Congress as follows.

On behalf of the Congress Board and the Danish Society of Oto-Laryngology I have the honour and pleasure to welcome you to this Seventeenth Congress of the Scandinavian Oto-laryngological Society

It is a special pleasure for the Society to welcome for the first time official members from Iceland to join our Society

This meeting will show several breaks of traditions. The motivation has been to secure as much unity in this gathering and in its scientific activities as possible. We have followed the rules of the classic French theatre: The unities of time, place and action. In our choice of topics we have aimed at demonstrating the scope of our field and our intentions to comply with demands from the subspecialities ranging under otolaryngology

As far as I know Scandinavian otolaryngologists met for the first time as members of the Section of Otology at the International Medical Congress, which was held in Copenhagen in 1884

Only 30 years later our Society was founded. Amongst its founders and its early members, three Danes are still alive, Blegvad, Mygind and Thornval.

In the hope that we shall be able to live up to that ardent enthusiasm which our predecessors entertained for otolaryngology and its Scandinavian co-operation I declare this Congress open.

Entertainments during the Congress

On Friday June 27 the members and their ladies were invited by the Danish Oto-Laryngological Society to a cocktail party and souper at the Marienlyst.

The banquet was held at the same place on Sunday June 29

On Saturday June 28 the ladies visited Copenhagen and had lunch at Tivoli.

On Sunday June 29 the ladies visited the Art Gallery Louisiana and had lunch at Restaurant Kystens Perle.

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MEETING OF THE COUNCIL OF THE SCANDINAVIAN OTO-LARYNGOLOGICAL SOCIETY

The meeting took place at the Marienlyst on June 27 at 11 a. m.

The following members of the Council were present. H C. Andersen, H K Kristensen and K. A. Thomsen representing Denmark T Palva and U Siirala representing Finland E. Thorsteinsson representing Iceland G Djupesland and T Leegaard representing Norway and G Herberts and G Nilsson representing Sweden.

The President of the Congress, Professor H C. Andersen was elected Chairman

G Herberts suggested that the next Congress should be held in Göteborg in 1972 The Council accepted the Swedish invitation with gratitude. It was proposed that Professor Gösta Herberts should act as President and Professor Hans Engström as Vice-President. This proposal was carried unanimously by the Council.

It was decided that the Past President, the Past Secretary and the Past Treasurer should always attend the meetings of the Council

The Council decided to recommend the business meeting to accept a Finnish proposal that in certain cases of "difficulties in communication" English should be accepted as an alternative Congress language.

BUSINESS MEETING OF THE CONGRESS

This meeting took place at Marienlyst on June 29 at 4 p m

The President announced the Swedish invitation for the next Congress to be held in Göteborg in 1972. The Congress accepted the invitation and unanimously agreed to the Swedish proposal that the next Congress Committee should consist of Professor G Herberts, President, Professor H Engström Vice-president, and Dr Hallén Secretary

Decisions upon the date, the programme and the publications of the transactions were left to this committee.

It was decided that the annual subscription fee should remain unchanged at the equivalent of 25 Swedish Kronor

It was decided that in special cases of difficulties of communication, a non-Scandinavian language may be accepted as an alternative Congress language.

The Bylaws of the Scandinavian Oto-Laryngological Society remained unchanged (printed in Acta-Otolaryng Suppl 224)

Acta Otolaryng. 263 3–7 1970

ELECTRON-MICROSCOPIC EXAMINATION OF THE INNER EAR OF THE PIGEON

G. F Dohlman

From the Department of Otolaryngology the University of Toronto, and the Defence Research Establishment Toronto Canada

The results are presented of electron-microscopic and experimental studies on the inner ear of the pigeon.

The relatively simple principle of the morphological and functional pattern in different parts of the inner ear is demonstrated. It is suggested that a comparison with equivalent structures in other species might be of value for their functional appreciation.

This presentation is intended to give a short survey of the mechanism of endolymphatic metabolism in the inner ear and as a preliminary report to evaluate the importance of the endolymph to the function of the sensory epithelium based on some recent findings and view points.

In the ampullae of the semicircular canals there are regions of specialized cells surrounding the hair-cell area on the cristae. They have been well known and morphologically described since the beginning of ear histology and have been generally believed to be secretory producing the endolymph filling the whole membranous inner ear One of these regions is the planum semilunatum, situated in the lateral wall of the ampulla seen in the microscope as a layer of high cylindrical cells. That these cells actually are secretory has previously been shown by means of autoradiography (Dohlman *et al.* 1959). Parenterally injected radioactive sulphur is accumulated in these cells in pigeons and later the labelled substances appear as a secretion in the endolymph. This secretion has been assumed to contain acid mucopolysaccharides based on the finding that they are labelled with sulphur and have been shown in the endolymph and cupula with appropriate staining techniques (Belanger 1961 Wislocki & Ladman, 1955) as well as chemically (Vilstrup *et al.*, 1955).

However the parenteral injections give a prolonged feeding through the blood supply to the cells to be studied. This makes it difficult to follow step by step the fate of the isotopes in the cell through the active organelles to the final secretional products. For this reason a "pulse labelling procedure has been used by injecting a small amount of the labelled isotope into the perilymph. The isotope is left in the perilymph surrounding the membranous ampulla for 2–3 minutes and is then removed by flushing with an artificial perilymph. Different time intervals between the exposure to the isotope and fixation in situ reveal the way through the membranous wall to the different organelles in the secretional cells and eventually the endolymph. Slide 1 is an illustration of some planum semilunatum cells "pulse-labelled" with radioactive sulphur and a time interval of 10 minutes. The autoradiographic silver grains are then found at the level of the Golgi apparatus of the cells.

However in order to study the nature of the secretion the pulse labelling" is also used for amino acids and sugars on the assumption that the secretional products are glycoproteins. Further other methods have been used to demonstrate the mucopolysaccharides in the pro-

Supported by grants from the National Research Council. Grant No 9III-279-50 and the Department of Supply and Services, Contract Ser GR 8–14.

ducts of the planum semilunatum cells. If treated with colloidal iron ruthenium red or lanthanum all these methods give the same results, showing vesicles conglomerating to vacuoles towards the endolymphatic surface of the cell. *Further with this method it* can be demonstrated that the secretion forms a network of mucopolysaccharides in the endolymph (Slide 2). In light microscopy the mucopolysaccharides can be seen in the endolymph as a loose network filling the whole endolymphatic system of the vestibular apparatus. In a section of the cupular substance (Slide 3) impregnated with colloidal iron the meshwork of the protein skeleton of the cupula chemically analysed by Iurato as belonging to the keratin group a *layer of polysaccharides* has been precipitated on all surface of the trabecles of the cupula and is partly found also in the spaces between them.

It has previously been pointed out that the cells on the slopes of the crista are morphologically different from those of the planum semilunatum (Dohlman 1964). Already Retzius saw them and described them as containing different kinds of cells. However Iwata (1924) called these parts of the walls "regiones secretoriae" and pointed out that these areas actually surround the hair-cell regions in the ampulla as well as the utricle. Ficandt & Saxén (1951) also mentioned morphological differences in these cell regions, but regarded them as a sign of different stages in a secretional cycle in the same way as it has been described for the goblet cells in the mucous membranes. However in the utricular walls there are also two kinds of cells. This has been described by Smith (1956). Dark and light cells on the slopes of the cristae in the guinea pig have also been described by Wersäll. In experiments some years ago in which the wall of the membranous ampulla had been cut resulting in an interchange between endolymph and perilymph it became evident that the dark cells changed in appearance. In electron-microscopy it could be seen that these cells were filled with large vacuoles.

As is well known Smith *et al* (1954) were able to analyse the labyrinthine fluids by modern methods. Their results showed that the sodium concentration in the perilymph was high and about the same as in all other extracellular fluids and the potassium content was correspondingly low. The endolymph is also an extracellular fluid but it showed a totally different composition with regard to these electrolyte ions. The endolymph has 30 times more potassium than the perilymph and 10 times less sodium.

A pertinent problem was therefore to find some methods to show the mechanism by which this unique electrolyte composition is created and maintained what structures are involved and the purpose of this strange electrolyte concentration.

When examined under the electron microscope the structure of the dark cells shows a thick brim of microvilli on the endolymphatic surface of the cells the cytoplasm is filled with mitochondria and the cell shows a labyrinth of indentations of the cell membrane at the base (Dohlman, 1965). All this is in accordance with a functional activity of moving fluid and solutes from the endolymph. Several methods were used to demonstrate the validity of this assumption. When methylene blue was injected into the endolymph, several distinct blue dots were found in the dark cells 1–2 minutes after the injection. After 10 minutes, small drops of the dye were seen to fill a great part of the cytoplasmic space when studied under the light microscope, and 1–1½ hours after the injections, methylene blue was found in the capillary walls. Injections of radioactively labelled sodium seemed also to indicate uptake in the dark cells, but these experiments must be reconfirmed to be significant. However if the dark cells absorb sodium, it would be reasonable to assume that these cells would contain more sodium than the surrounding cells. On this assumption, the sodium was precipitated with antimony compounds by the method of Komnick (1962). Together these different experiments appear to indicate that

the dark cells selectively remove sodium from the endolymph.

It is, however generally accepted that "pumping" of sodium in one direction is accompanied by an equivalent movement of potassium ions in the opposite direction. This would then result in an increase in potassium and a depletion of sodium in the endolymph. This is a highly energy-consuming process. As is well known, the mitochondria are the main producers of energy for the functions of the cells. The enormous amount of mitochondria in the dark cells indicates the high production of energy by these cells, explaining the origin of energy for their function as an ion-exchange "pump".

The areas containing dark cells surround the sensory cell regions in all the ampullae as well as the utricle. This seems to indicate that the function of the dark cells which appear to create this unique potassium-sodium concentration of the endolymph must be of great importance to the function of the sensory cells. It is also well known, from the investigations of Davis *et al.* (1955) and many others, that an increase in sodium concentration as well as a decrease in potassium are harmful to the function of the hair cells and can even be dangerous to the survival of these cells.

The cells for the creation and maintenance of this special electrolyte concentration in the ampullae therefore seem to be concentrated in the regions close to the cristae and around the maculae. However it would be of considerable importance to know if and how this ion concentration can be maintained also in other areas of the endolymph system at some distance from the dark-cell areas, for example, in the relatively long semicircular canals. It would seem reasonable if some leakage of ions would occur through the thin membranous canal walls separating endo- and perilymph (Meyer 1951) with the high difference in concentration of ions in these two fluid systems.

Some experiments were therefore performed (Dohlman & Radomski, 1968) to investigate the ability of the membranous canal walls to maintain the ion concentrations in the endolymph.

1. The anterior canal of the pigeon was clamped at both ends after special precautions to maintain the vascular blood supply to the canal. In these experiments, the potassium concentration remained unchanged even after a period of 3–4 hours.

2. The canal together with the blood vessels were clamped at both ends of the canal. Then the potassium concentration fell rapidly and became equal to the perilymph within 2–2½ hours.

3. The endolymph of the canal was substituted with a solution of an artificial perilymph. The canal was then clamped, but the vascular supply was left intact. In this case, there was a slow increase in the potassium content in the canal.

Thus, these experiments have evidenced that even in the canals with its flat and thin "indifferent" epithelium the ability to maintain the specific ion concentration of endolymph is present. It might therefore be assumed that the non-specific epithelium of all the walls of the membranous inner ear have this same functional ability.

Between the dark cells are cells with a much lighter cytoplasm. These cells have no microvilli, but a large Golgi apparatus and vesicles and inclusions indicating a secretional function. Experiments with colloidal iron and other methods of staining mucopolysaccharides proved that they were secreting these substances.

It has been shown by several investigators that the electrolyte concentration is the same in the endolymph when taken from the vestibular apparatus and from the cochlea, the two parts of the inner ear without a functional communication. It must therefore be of importance to investigate the morphology first of all the cells responsible for the ion exchange, the dark cells, secondly also the light cells with the ability to produce a secretion into the endolymph, and finally to compare these two cell types and their function in the two parts

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It is, however generally accepted that "pumping of sodium in one direction is accompanied by an equivalent movement of potassium ions in the opposite direction. This would then result in an increase in potassium and a depletion of sodium in the endolymph. This is a highly energy-consuming process. As is well known, the mitochondria are the main producers of energy for the functions of the cells. The enormous amount of mitochondria in the dark cells indicates the high production of energy by these cells, explaining the origin of energy for their function as an ion-exchange pump"

The areas containing dark cells surround the sensory cell regions in all the ampullae as well as the utricle. This seems to indicate that the function of the dark cells which appear to create this unique potassium-sodium concentration of the endolymph must be of great importance to the function of the sensory cells. It is also well known, from the investigations of Davis *et al.* (1955) and many others, that an increase in sodium concentration as well as a decrease in potassium are harmful to the function of the hair cells and can even be dangerous to the survival of these cells.

The cells for the creation and maintenance of this special electrolyte concentration in the ampullae therefore seem to be concentrated in the regions close to the cristae and around the maculae. However it would be of considerable importance to know if and how this ion concentration can be maintained also in other areas of the endolymph system at some distance from the dark-cell areas, for example, in the relatively long semicircular canals. It would seem reasonable if some leakage of ions would occur through the thin membranous canal walls separating endo- and perilymph (Meyer, 1951), with the high difference in concentration of ions in these two fluid systems.

Some experiments were therefore performed (Dohlman & Radomski, 1968) to investigate the ability of the membranous canal walls to maintain the ion concentrations in the endolymph.

1. The anterior canal of the pigeon was clamped at both ends after special precautions to maintain the vascular blood supply to the canal. In these experiments, the potassium concentration remained unchanged even after a period of 3–4 hours.

2. The canal together with the blood vessels were clamped at both ends of the canal. Then the potassium concentration fell rapidly and became equal to the perilymph within 2–2½ hours.

3. The endolymph of the canal was substituted with a solution of an artificial perilymph. The canal was then clamped, but the vascular supply was left intact. In this case, there was a slow increase in the potassium content in the canal.

Thus, these experiments have evidenced that even in the canals with its flat and thin "indifferent" epithelium the ability to maintain the specific ion concentration of endolymph is present. It might therefore be assumed that the non-specific epithelium of all the walls of the membranous inner ear have this same functional ability

Between the dark cells are cells with a much lighter cytoplasm. These cells have no microvilli, but a large Golgi apparatus and vesicles and inclusions indicating a secretional function. Experiments with colloidal iron and other methods of staining mucopolysaccharides proved that they were secreting these substances.

It has been shown by several investigators that the electrolyte concentration is the same in the endolymph when taken from the vestibular apparatus and from the cochlea, the two parts of the inner ear without a functional communication. It must therefore be of importance to investigate the morphology first of all the cells responsible for the ion exchange, the dark cells, secondly also the light cells with the ability to produce a secretion into the endolymph, and finally to compare these two cell types and their function in the two parts

ducts of the planum semilunatum cells. If treated with colloidal iron ruthenium red or lanthanum, all these methods give the same results, showing vesicles conglomerating to vacuoles towards the endolymphatic surface of the cell Further with this method it can be demonstrated that the secretion forms a network of mucopolysaccharides in the endolymph (Slide 2) In light microscopy the mucopolysaccharides can be seen in the endolymph as a loose network filling the whole endolymphatic system of the vestibular apparatus In a section of the cupular substance (Slide 3) impregnated with colloidal iron the meshwork of the protein skeleton of the cupula chemically analysed by Iurato as belonging to the keratin group a layer of polysaccharides has been precipitated on all surface of the trabecles of the cupula and is partly found also in the spaces between them

It has previously been pointed out that the cells on the slopes of the crista are morphologically different from those of the planum semilunatum (Dohlman 1964) Already Retzius saw them and described them as containing different kinds of cells. However Iwata (1924) called these parts of the walls "regiones secretoriae" and pointed out that these areas actually surround the hair-cell regions in the ampulla as well as the utricle. Ficandt & Saxén (1951) also mentioned morphological differences in these cell regions, but regarded them as a sign of different stages in a secretional cycle in the same way as it has been described for the goblet cells in the mucous membranes. However in the utricular walls there are also two kinds of cells. This has been described by Smith (1956) Dark and light cells on the slopes of the cristae in the guinea pig have also been described by Wersäll In experiments some years ago in which the wall of the membranous ampulla had been cut resulting in an interchange between endolymph and perilymph it became evident that the dark cells changed in appearance In electron microscopy it could be seen that these cells were filled with large vacuoles.

As is well known Smith *et al* (1954) were able to analyse the labyrinthine fluids by modern methods. Their results showed that the sodium concentration in the perilymph was high and about the same as in all other extracellular fluids, and the potassium content was correspondingly low The endolymph is also an extracellular fluid but it showed a totally different composition with regard to these electrolyte ions. The endolymph has 30 times more potassium than the perilymph and 10 times less sodium.

A pertinent problem was therefore to find some methods to show the mechanism by which this unique electrolyte composition is created and maintained what structures are involved and the purpose of this strange electrolyte concentration

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of the inner ear This comparison appeared to be more easily interpreted in the simple ear of the pigeon than in higher animals.

In the cochlea of birds, the part of the wall in the cochlear duct which corresponds to the stria vascularis in mammals is the so-called tegmentum vasculosum Already in light microscopy it is seen that this structure is composed of the regular sequence of dark and light cells demonstrated in the vestibular apparatus. This has also recently been pointed out by Jahnke *et al* (1969) In electron microscopy it is evident that the dark cells have the same characteristics as those in the ampullae a brim of microvilli the cytoplasm is filled with mitochondria, and the base of the cell is deeply indented Experiments with methylene blue shows the same uptake of the dye in the vacuoles, and this can be confirmed under the electron microscope. In all probability the dark cells in the two parts of the ear therefore appear to have a basically similar function.

The light cells in the cochlea, however show some significant differences as compared with those in the vestibular apparatus. They appear more "empty" they have a small Golgi apparatus and only a few inclusions, mostly in the upper parts of the cell, close to the endolymphatic surface. However that they are secreting cells is demonstrated in Slide 4 showing a rounded droplet just passing through the cell membrane. In this case, the droplet contains lipids, confirmed by staining with Sudan black but there are other adjacent inclusions which also seem to be on their way to extrusion. Treated with colloidal iron these cells show very little of mucopolysaccharides in their secretional products

In conclusion these studies have shown that the whole endolymphatic system is well supplied with epithelial cells with special functions. The most important seems to be the dark cells, which have the ability to remove sodium from the endolymph and at the same time increase the potassium concentration. It is well known that this is a necessary condition for the function of the hair cells, which explains the location of the dark cell areas in closest vicinity to the different regions of sensory cells.

It has been assumed by several investigators that the endolymph should have the function of carrying nutrients and oxygen to the hair cells. This assumption is based on the misconception that the hair cells in the organ of Corti had no access to a direct nutrition from blood capillaries. Those which were found in the vicinity the spiral vessels, seemed to be too far away from the cells to provide a sufficient nutritional supply The experiments by Lawrence (1966) showed that a blocking of these spiral vessels under the organ of Corti resulted in a destruction of the hair cells in spite of an intact stria vascularis. On the other hand, a destruction of the stria vascularis had no effect on the hair cells. The sensory cell areas of the vestibular apparatus are all well supplied by a highly developed capillary network. This excludes the possibility of any hypothetical bypass over the endolymph as a route for nutrition of their hair cells. To assume one mechanism for nutrition of the vestibular hair cells from the adjacent capillaries and another through the endolymph for the cochlear sense organ therefore seems rather far fetched. Further the investigations by Silverstein (1966) has evidenced that the glucose concentration of the endolymph is only one tenth of that of the blood. Finally Misrahy's measurements of the oxygen tension in the cochlea showed that close to the hair cells the values were so low that they must be regarded as incompatible with an oxygen uptake from the endolymph (Rauch, 1966)

One important problem is the role of the mucopolysaccharides in the vestibular part of the cochlear endolymph This finding seems to contradict any vital importance of these substances for the direct stimulatory function of the hair cells, if they are present in one part and absent in the other The hair cells must be assumed to demand the same environmental conditions for their stimulation. However the conditions in the vestibular apparatus for transmission of mechanical energy would seem

to be favoured by a meshwork of polysaccharides. If they fill the canals in continuity with the cupulae, it seems probable that they are moved as an intimately bound unit in their responses to angular accelerations, whereas a gel-like condition of the endolymph in the cochlea responding to the rapid fluctuations to tones and sound probably would be a functional disadvantage.

Finally from a morphological point of view this study aimed at showing the simplicity in the arrangement of the two main cell types of the specialized epithelium in the whole inner ear. The dark ion-exchanging and the light secretional cells are everywhere located in the closest vicinity to the sensory cell areas. The clearly separated dark and light cells in the primitive cochlea of the pigeon with their distinctly separated functions might therefore serve as a simple pattern of the more complicated stria vascularis in higher animals.

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THE RADIOLOGIC DIAGNOSIS OF OTOSCLEROSIS

H Rovsing

From the Radiological Department University Hospital Copenhagen, Denmark

Tomography employing Philips Massiot's Polytome in the semi-axial and the axial-pyramidal projection allows tomographic demonstration of fenestral and retrofenestral otosclerosis, respectively. Examples of otosclerotic changes in the labyrinthine windows, the promontory and the fossula of the vestibular window are demonstrated. The tomographic difference between active and inactive otosclerosis is shown and the pathological changes of the cochlea compatible with the diagnosis of retrofenestral otosclerosis are demonstrated along with some cases of re-impaired hearing following stapedectomy by the method of Schuknecht in which re-obliteration of the vestibular window or dislocation of the wire has been diagnosed tomographically

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THE IBSEN-MACKEPRANG COLLECTION

TOMOGRAPHY AND PHOTOGRAPHY

J. Jensen and L. Hansen

From the Radiological Department, University Hospital, Copenhagen, Denmark

The Ibsen-Mackeprang Collection was created in the period from 1874 to 1937 and comprises 101 admirably prepared temporal bones from deaf children. Of the specimens 36 present abnormalities within the labyrinth. In 18 of these the changes must be regarded primarily as developmental anomalies. In the remaining 14, the changes consists of osseous obliteration, either of the entire labyrinth, or parts of it. In the specimens with obliteration, the origin of deafness was postnatal in 14. In the remaining four the origin of deafness was unknown; in two the children were stated to be born deaf.

Nine specimens reveals Mondini malformation, i.e. hypoplasia of the axial skeleton of the cochlea, resulting in only 1 coils. In one of the temporal bones aplasia of the posterior semicircular canal is present, and in two the internal acoustic meatus is malformed.

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OTO-PATHOLOGICAL EXAMINATION OF OTOSCLEROSIS AND NEURINOMATA OF THE ACOUSTIC NERVE

M Balslev Jørgensen, P Bretlau U Ebert and E. Hentzer

From the Oto-Pathological Laboratory University Hospital Copenhagen, Denmark

The exhibition from the oto-patological laboratory demonstrates:

1 Different localisation and activity of the otosclerotic focus.

2 Lateral neurinomata of the acoustic nerve
   a. localised in the meatus acousticus internus
   b rare cases localised inside the modiolus and the scala typmani.

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LABYRINTHEMBRYOLOGY

J Falbe-Hansen

From the Department of Otolaryngology Municipal Hospital Copenhagen, Denmark

An exhibition of photomicrographs from the developing labyrinth in man, guinea pigs, albino rats and pigs.

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THE PHYSIOLOGY OF THE EUSTACHIAN TUBE – FILM

S Ingelstedt

From the Department of Otolaryngology University Hospital Lund Sweden

The normal tubal function is quantitatively evaluated on a film at varied controlled pressure changes in side and outside the middle-ear cavity The methods for such determinations are based on recordings of the movements of the intact ear drum. The aim is to show that such measurements performed during the conditions defined give possibilities of determining the volume of the air filled ear space the elastic proper ties of the tympanic membrane, the events during changing ambient pressure or during the act of opening the tube

DISCUSSION

M Tos

Mucous Glands and Goblet Cells in the Eustachian Tube

I should like to call attention to the mucous elements in the Eustachian tube. It contains about 40 sero-mucous glands and numerous goblet cells in the epithelium The secretion produced by these mucous elements passes into the tubal lumen The role of these mucous ele ments in tubal function is still unknown It might well be imagined that in catarrhal con ditions hypersecretion of the mucous glands and of the goblet cells occurs resulting in an increase of tenacious secretion in the tube. This may entail tubal stenosis without any thickening of the mucosa or other abnormalities. It might also be imagined that in chronic catarrhal conditions there would be an increase in the gland mass in the tube and an increased number of goblet cells as in the trachea and bronchi in chronic bronchitis The tubal mucosa is similar to that of the nose and lower air ways. Just as the mucous secretion in these sites increases in catarrhal conditions, the same may also apply to the Eustachian tube. Now and then, rustling of secretion in the tube may be heard in Politzer s manoeuvre or during insufflation of air

In the Glostrup Hospital Copenhagen, we are studying the development, structure, and distribution of the mucous elements of the Eustachian tube This is being done by whole-mount methods in which the entire tube is dissected free, presenting itself as a thin tube consisting of mucosa and submucosa (Fig 1). The entire tube with the middle ear is then stained *in toto* by the PAS-Alcian blue whole mount method. The mucous glands manifest themselves as blue, branched structures, the gland mass in the submucosa and the excretory duct debouching into the tubal lumen (Fig 1) The goblet cells stand out as intensely blue-stained, round spots in the epithelium.

The development of the glands starts at the pharyngeal end of the tube in the 13th week of pregnancy The glandular primordia grow down into the submucosa where they undergo dichotomous division several times, forming tubules and acini The glands are present only in the pharyngeal half of the tube, with the greatest density around the pharyngeal orifice

The goblet cells start forming in the 14th week of pregnancy also at the pharyngeal end whence they continue towards the middle ear Throughout foetal life the density of the goblet cells is greater in the pharyngeal than in the tympanic half of the tube. At birth



Fig. 1. Eustachian tube from foetus aged 21 weeks. PAS-Alcian blue-stained whole-mount (× 35). The tube is 4 mm in length and 0.5 mm in diameter. Several glands (arrows) are already quite widely branched and situated in the submucosa. In the epithelium, many dark patches which represent groups of goblet cells are visible. The goblet cells are densest in the pharyngeal half (P), but also continue towards the hypotympanum (H). In other parts of the middle ear (T) there are only few goblet cells.

and during infancy the density of the goblet cells has already reached a maximum.

The object of these studies is to elucidate the anatomy of the mucous elements and to determine the density of goblet cells in a normal series. This is to form the basis of quantitative studies of the mucous elements in disease, such as acute otosalpingitis, adhesive otitis, and chronic otitis media.

U. Sibrula: In a few cases of adhesive otitis we have succeeded in maintaining the operatively created air-filled tympanum by permanent insufflation with water saturated air.

EUSTACHIAN TUBE FUNCTION ASSESSED WITH TYMPANOMETRY

A NEW TESTING PROCEDURE IN EARS WITH INTACT TYMPANIC MEMBRANE

J Holmquist

From the Department of Otolaryngology and the Laboratory of Audiology Sahlgren s Hospital University Göteborg Sweden

A testing procedure allowing rapid and physiological determination of the tubal function in ears with intact ear drum is introduced. Testing results in normal as well as pathological ears are presented and discussed. The procedure seems to objectivize tubal function disorders which we have previously been unable to determine in clinical routine

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POSTURE AND EUSTACHIAN TUBE FUNCTION

H. Rundcrantz

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The patency of the Eustachian tube is affected by the position of the body a phenomenon observed particularly in patients with patulous tubes. The symptoms of acute otitis media often start at night when the patient has been in bed for some hours. These facts indicate that the horizontal body position may constitute factor contributing to the development of acute or chronic otitis media. The ventilatory capacity of the Eustachian tube has been studied in different postures. The clinical consequences of postural effects on the Eustachian tube are discussed.

During upper respiratory infections some symptoms often begin or grow worse at night a few hours after the patient has gone to bed. All of us have certainly noticed decreased nasal patency in the recumbent position during a common cold. It is also a well-known clinical fact that the symptoms of acute otitis media often start at night, and that the symptoms are sometimes alleviated when the patient gets up.

About 100 years ago it was first shown (Lucae, 186 Hartmann, 1879) that different positions of the head and different postures affected the patency of the Eustachian tube. In his by now classical investigations on healthy persons and patients with patulous tubes, Perlman (1939) found that the air flow through the tube was always impaired in the recumbent position. Perlman thought that during sleep at night the Eustachian tube should be considered impermeable

Impairment or interruption of the essential air contact between the middle-ear cavity and pharynx through the Eustachian tube during an upper respiratory infection contributes to the development of acute or serous otitis media. The medical literature contains only stray comments on the increased frequency of symptoms at night, which are typical of acute otitis media, and the factors underlying the phenomenon have not been analysed. Nor are they—as a rule—considered in connection with the treatment of the disease.

Problem

Adult man spends about 8 hours every night in the horizontal position, small children even more. Patients with common colds are often advised to go to bed for a couple of days to cure the illness. To what extent is the normally patent tube affected by a change in the body position from the vertical to the horizontal level? How is the tube in various postures affected if the patient suffers from an upper respiratory infection?

METHOD

Fig. 1 shows a middle-ear model. In the bony part of the ear canal (cc) a polyethylene catheter is inserted and fixed air-tight. The tympanic membrane is perforated. Special arrangements with an electric fan can produce a constant negative or positive intratympanic pressure (Pm) through the catheter. When the tube opens during deglutition, an air volume will pass through the tube and also through the catheter (Vt).

The walls of the middle-ear space are prin-

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of air passing through the Eustachian tube during deglution during health and infection. The decrease of tubal patency during infection, seen already in the erect position, became very marked in the 20° position. In the recumbent position, none of the subjects could open their tubes at all. After 10 minutes in this position, the tubal function did not recover until after 10–35 minutes in the erect position.

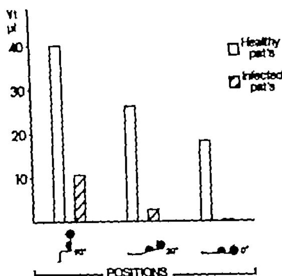


Fig. 4. The mean values of Vt in different positions in five subjects during health and infection.

CONCLUSIONS

In subjects with normal tubal function, a change in the body position from the erect to the horizontal level causes a decrease in tubal patency to one third of that in the erect position. In a position of 20° above the horizontal plane, the patency decreases to only two thirds. This phenomenon is proved to be caused by the hydrostatic venous capillary congestion of the mucosa of the middle ear and the Eustachian tube. During upper respiratory infections, this positional effect is much more pronounced, so that the tube seems to be occluded in a body position below 20° above the horizontal plane. A rapid development of atelectasis of the middle ear will take place, which paves the way for middle-ear disease.

It would therefore be logical to recommend patients with common colds, especially children with a history of recurrent acute or serous otitis media, to take up a position during bed rest of not less than 20 above the horizontal plane in order to prevent tubal occlusion. The same advice should be given in the postoperative period to patients submitted to tympanoplastic surgery

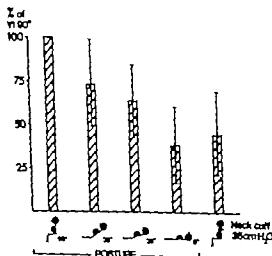


Fig. 3. The percentual mean values and S. D. of Vt in different positions and during neck-vein compression in healthy subjects.

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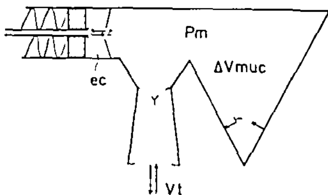


Fig. 1 The principal arrangement of measuring the air volumes passing through the Eustachian tube (Vt) and the changes in volume of the middle-ear space (Δ Vmuc).

cipally rigid but changes in its volume (Δ Vmuc) appear as the result of variations in the capillary venous engorgement in the tympanic mucosa. Δ Vmuc also produces small air flows through the catheter which is connected to an electronic measuring device capable of recording Vt as well as Δ Vmuc with high accuracy expressed in terms of μl.

Sixteen persons with dry central perforations of the tympanic membrane were investigated. All of these could easily equilibrate negative and positive intratympanic pressures of 2 cm H_2O In the investigation constant positive pressures of 2 or 4 cm H_2O were used The subjects were asked to swallow once a minute during 10 minutes in different body positions. Vt was recorded on every deglutition, Δ Vmuc

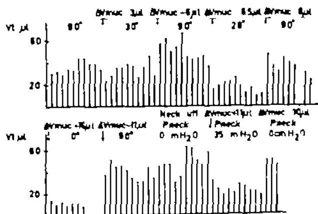


Fig. Vt and Δ Vmuc in one subject in different positions and during neck vein compression (Pneck 35 cm H_2O)

was recorded on every change in posture The positions investigated were sitting erect, reclining 30° and 20° above the horizontal plane, and finally lying down horizontally

RESULTS

Fig. 2 shows the results in one patient The closer to the horizontal plane the subject was placed the more did Vt decrease Δ Vmuc, the volume change in the middle-ear space due to different capillary venous engorgement, was also proportional to the degree of the change in body position Jonson & Rundcrantz (1969) made catheterizations and pressure recordings inside the bulb of the internal jugular veins of healthy individuals. In the sitting position the pressure was nearly zero When the body position was changed towards the horizontal level, the venous pressure began to increase at the angle of 20° and in the horizontal position it was about 10 cm H_2O This pressure was directly proportional to the level between the right auricle of the heart and the bulb The same venous pressure could be produced in the sitting position if a torniquet was applied round the neck and inflated to 35 cm H_2O Such a venous compression also caused a decrease of Vt as seen in Fig. 2.

The mean values of the air volumes passing through the Eustachian tubes in different positions and during neck vein compression were calculated for the entire series. The values were expressed as the percentage of Vt in the sitting position (Fig 3) Reclining 30° above the horizontal plane caused a reduction of tubal patency to 73 % in the 20 position the values decreased to 64 % and in the horizontal position the patency of the tube was only 38 % of the mean value in the sitting position During neck vein compression the tubal patency was reduced to 44 %

Five of the patients fell ill with upper respiratory infections in the course of the investigation and could be re-examined during the infection. There was, however no signs of middle ear infection Fig 4 shows the mean volumes

Very likely the type of patulous tube condition that appears during pregnancy and with the use of preventive pills (Allen, 1967) is also due to a mucous membrane affection.

The extraluminal factors include changes in muscles, cartilage and other tissues around the lumen of the Eustachian tube. Ostmann (1893) studied how atrophy near the tube could affect its patency. It is also well known that loss of weight with reduction of fat and subsequent reduced tissue pressure can give rise to a patulous tube condition.

After operations on the epipharynx or near the Eustachian tube a patulous condition may arise because of adhesions directly or indirectly affecting the mechanism of opening and closing the Eustachian tube. Radiological treatment of epipharynx tumours may also result in a patulous tube owing to postradiological changes.

It was shown by Politzer (1861) and later by Rich (1920) that the Eustachian tube is opened by the tensor veli palatini muscle, probably with the aid of the levator veli palatini muscle. Occasionally this muscle mechanism can be systematically trained, so that the Eustachian tube may be opened voluntarily (Wersäll, 1964).

The patulous tube may also be due to a combination of luminal and extraluminal factors. An example of this can be seen in cases with chronic otitis. Zöllner (1942) and Flisberg (1966) showed that the condition may be more common in patients with chronic otitis. The reason for this is likely to be a combination of mucous membrane changes and fibrotic changes in the tissues around the tubal lumen caused by the chronic infective condition. Perlman (1939) proved that a patulous tube could arise after retrogasserian neurectomy performed to relieve trigeminal neuralgia. He thought that a lack of tonus of the muscles that affect the Eustachian tube (tensor veli palatini muscle) and are supplied by the fifth nerve is the principal factor in producing the clinical entity. However Haodi (1959) and Flisberg (1966) expressed the view that a certain influence on the mucous membrane may also contribute to the patulous state of the Eustachian tube after this operation.

PRESENT INVESTIGATIONS

Material

A retrospective investigation was made covering all patients with a diagnosis of patulous tube in the ENT Department, Lund, since 1964. A total of 90 cases of unquestionable patulous tube condition were found, verified by Eustachian tube function test. Fifty-three of these cases, i.e. 63 % were women. There were five patients in the series who had been operated on with retrogasserian neurectomy because of trigeminal neuralgia, six had chronic otitis media, and six women stated that they used oral contraceptive preparations. Questionnaires were sent to all patients in whom the condition had been diagnosed during 1967 and 1968 (50 patients) inquiring about their symptoms.

Method

To elucidate the mechanisms and solve the problem why the symptoms sometimes disappear for example, in the recumbent position, a further investigation was made in some of the patients. At nasal respiration, recordings were made of the pressure changes in the nose and the middle ear across the intact ear drum in different body positions. The equipment used has previously been described in detail by Ingelstedt *et al* (1967).

Results

Answers were given by 34 of the 50 patients asked. In five answers, spontaneous improvement of all symptoms was stated. The improvement had followed a certain weight increase or the end of pregnancy. There was no chronic otitis media or operatively induced patulous tube among the patients. *Table 1* gives the frequency of positive symptoms in the remaining 29 patients. The most common symptom—feeling of deafness in the ear—was mentioned by 19 of the patients. This symptom was felt in the erect position, but only one patient had trouble also at night or when lying down.

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MIDDLE EAR MECHANICS IN PATULOUS TUBE CASES

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Over a 5-year period 90 cases with patulous tube conditions verified by Eustachian tube function tests were found at the ENT Department of Lund. Sixty-three per cent of these were women. By questioning the various symptoms could be evaluated. To elucidate the factors which might relieve the symptoms, simultaneous pressure recordings in nose and middle ear were made in some of the patients. Two factors seemed to relieve the symptoms: an increase of the hydrostatic pressure in the head and a relative under pressure in the middle ear

The patulous Eustachian tube was described for the first time 1864 by Schwartze who observed that a scarred ear drum moved synchronously with the breathing. A more complete report of the condition was given by Jago (1867) He had himself had right sided patulous tube trouble. Not until Jago increased in weight by $^1/_7$ of his original weight did the symptoms disappear The same happened now and even earlier "for several hours after a hearty meal" Except for occasional reports, little attention was paid to the patulous tube condition until the 1930's when it was discussed by Pitman (1929) Zöllner (1937) Shambaugh (1938) and Perlman (1939) For some years, several authors have called attention to the patulous tube condition and also discussed aetiology symptomatology and treatment, inter alia Metz (1953) Moore & Miller (1961) Miller (1961) Pulec & Simonton (1964) and Allen (1967)

Symptoms

The symptom often seem to be paradoxical, as many of them resemble the symptoms seen in obstruction of the Eustachian tube This certainly contributes to a common tendency to overlook the condition The patulous tube has actually proved to be considerably more common than has previously been realized.

The symptoms are

1 Feeling of head as "in an empty barrel" (feeling of deafness in ear)
2. *Autophony*
3 Tinnitus.
4 Feeling of one's own breathing in the ear
5 The symptoms may be aggravated by exercise, fatigue and nervousness.
6 The symptoms may be aggravated by loss of weight or start after loss of weight.
7 The symptoms may be relieved by upper respiratory infection.
8 The symptoms may be relieved by the horizontal position.
9 The symptoms may be relieved by sharp "sniffing"

Aetiology

Theoretically the condition of the patulous tube state may be caused by luminal factors, extraluminal factors or a combination of both

The luminal factors include different types of mucous membrane changes. These factors probably play an important role in the regulation of the patency of the tube. In most cases, the simple procedure to ask the patient to lie down eliminates patulous tube trouble. This is due to the increasing degree of filling of the veins and lymphatic vessels owing to the higher hydrostatic pressure in the head in the horisontal position.



Fig. 3. Pressure recordings in the same case as in Fig. 1 and 2. The patient placed horizontally. At the arrow the Eustachian tube has closed – level of the middle-ear pressure curve.

inspiration phase when the tendency of the Eustachian tube to close, because of the hydrostatic factor was increased by the pressure relations in nose and ear causing a sucking effect. When the Eustachian tube was closed, this could be recorded as a levelling of the middle ear pressure curve. The pressure in the middle ear was then always negative

DISCUSSION

The patulous tube has previously been considered a rather unusual condition. In recent years, interest has more and more tended to focus on the clinical entity. This is probably the reason why an increasing number of cases have been reported.

Of special interest are the patulous cases with follow retrogasserian neurectomy. According to Perlman (1939), this type of patulous tube is chiefly caused by extraluminal factors, "lack of muscle tonus". An objection to this theory is the fact that the Eustachian tube is opened by the very muscle which at this operation is in danger of losing its innervation. However, according to Graves & Edwards (1944), the sensory innervation to the pharyngeal orifice of the Eustachian tube can also be innervated by the trigeminal nerve (normally by the glossopharyngeal nerve). After retrogasserian neurectomy an atrophy of the mucous membrane of the same side of the nose may be combined with a patulous tube. This would then be due to trophic disturbances of the mucous membrane of the Eustachian tube.

During the medication of oral contraceptive preparations there is an increase in the level of oestrogen in the blood (just as in pregnancy). The oestrogen affects the mucous membrane of the nose and epipharynx either directly or indirectly via the pituitary gland (Schiff, 1959). It could be mentioned by way of comparison that oestrogen not only affects the thickness of the mucous membrane of the genital tract, but also that the secretion from the cervix uteri becomes thinner and the cervix dilated due to this hormonal action. The hormonal influence seems to cause a patulous tube condition as a side effect in certain cases.

During the investigation of a patient with a patulous tube in different body positions it was observed that the Eustachian tube varied with body position as well as with pressure relations in the nose and middle ear. A horizontal body position always closed the Eustachian tube because of the increased hydrostatic pressure in the mucous membrane of the head. The same tendency was observed when a relative under pressure in the middle ear was built up. Such a pressure relation tends to close the lumen of the Eustachian tube. This type of pressure relation appears at inspiration. Patients with patulous tube use this phenomenon to get rid of the symptoms by performing a so-called "sniffing or reverse Valsalva manoeuvre". Conversely a higher pressure in the nose than in the middle ear tends to dilate the Eustachian tube as previously demonstrated by Flisberg (1966). In the study of normal individuals during tubal function test it could be observed that the Eustachian tube was periodically open. This often happens when the patient has performed Valsalva's manoeuvre, during which the Eustachian tube had been opened and dilated. Probably the same takes place now and then normally and the state of patulous tube can then hardly be regarded as pathological.

The symptoms of patients with patulous tubes might be curious as well as unpleasant. Often the patients' trouble has, furthermore, been neglected at one or several examinations. When the diagnosis is established, most patients are content with the information that it is a quite

Table 1 *Positive symptoms in a material of patients with patulous tube condition*

	Men	Women	Total
Number	8	21	9
Age in years	18–35 (mean 30)	17–77 (mean 42)	17–77 (mean 39)
Symptoms:			
Feeling of deafness in ear			
lying	0	1	1
upright	7	1	19
Tinnitus	1	11	1
Autophony	3	12	15
Breathing heard in ear	4	13	17
Aggravation at stress, fatigue and exercise	5	11	16
Symptoms starting at weight loss	2	7	9
Relief of symptoms at common cold	3	4	7

Figs. 1–3 show the pressure changes which could be recorded in a patient with a patulous tube in different body positions.

In Fig. 1 with a patient in the erect position the pressure changes in the nose and middle ear practically agree with only a small delay of the middle-ear pressure in relation to the pressure in the rhinopharynx. At expiration (a) there were the same pressure in the nose and the middle ear (+ 1 8 cm H O) Because of this positive

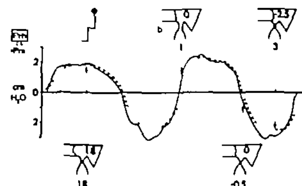


Fig. 1 Pressure recordings in nose (P_{rh}) and middle ear (P_m) at nasal respiration in a patulous tube case (woman, 18 years old) in the erect position
At (a) expiration (b) zero level at change between phases of inspiration and expiration ( ) zero level change between phases of expiration and inspiration (d) inspiration. a brief closing of the Eustachian tube is seen as a levelling of the middle-ear pressure curve

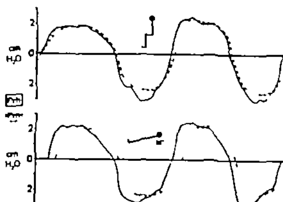


Fig. 2. Pressure recordings in the same case as in Fig. 1 Upper curve: the patient placed in the erect position. Lower curve: the patient placed with head 25 above the horisontal plane.

pressure the ear drum bulged outwards. At the stage between the inspiration and expiration phases (b) the pressure in the nose was positive —here + 1 cm H_2O—when the pressure in the middle ear was zero which meant a normal ear-drum position at that very point. This pressure relation gave a slight dilatation of the Eustachian tube, which was also the case at (a) with positive pressures in nose as well as middle ear When the pressure in the nose was lower than in the middle ear which was the case at (c) and (d) the reverse took place i. e. a tendency of the Eustachian tube to become narrower or to close. In fact, the tube closed at (d) which could be seen as a straight line in the middle-ear pressure curve during the maximum of inspiration.

In Fig. 2 the upper curve shows the pressure changes when the patient was in the erect position. Lower curve the patient was placed with his head in a position 25 above the horisontal plane according to the findings of Rundcrantz (1969) A moderate delay of the middle ear pressure was the result. This delay was an expression of the tendency of the Eustachian tube to close because of the increased pressure in the mucous membrane vessels The delay was seen as a *time displacement* of the middle-ear pressure curve on the abscissa.

In Fig. 3 the patient was placed horisontally Then a marked delay of the middle-ear pressure could be seen up to the closing of the Eustachian tube. This closing always took place at an

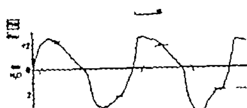


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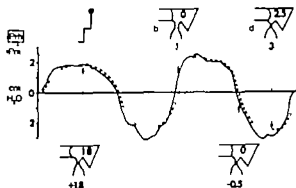


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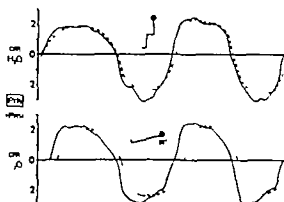


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In Fig. 3 the patient was placed horizontally Then a marked delay of the middle-ear pressure could be seen up to the closing of the Eustachian tube. This closing always took place at an

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TUBAL FUNCTION IN PATIENTS WITH CHRONIC SECRETORY OTITIS MEDIA

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Tubulation of the middle ear in patients with chronic secretory otitis offers an opportunity to evaluate the tubal function by means of aspiration by the method of Flisberg. The tubal function was followed in 18 patients by this method for 6 months and was found to be definitely inferior to normal values as given by Holmquist.

The aetiology of chronic secretory otitis media is still under discussion. Most investigators agree that the tubal function is of major importance, which is also implied by the fact that removal of adenoids is recommended as the first procedure in the treatment of this condition.

This report presents an attempt to evaluate the tubal function in children with secretory otitis media of long duration. There are a number of methods by which the tubal function can be determined. The so-called indirect methods are widely used, but can only be applied when the tympanic membrane is intact and the middle-ear space contains air. Flisberg *et al* (1962) developed a very promising method, the so-called aspiration method, which, however requires that there is a perforation of the tympanic membrane.

They applied a negative pressure in the ear canal, and the criterion was how far this pressure would be reduced by repeated swallowing, or in other words, the minimum pressure gradient between the nasopharynx and the middle ear that would still produce an opening of the tube during swallowing. Holmquist (1968) used this method in a number of patients with perforations of the eardrum and correlated the findings to the clinical results obtained by myringoplastic operations. One group of patients were able to reduce the ear canal pressure to −100 mm water or less. Here the operation was a complete success in 75 % against only in 12 % of the patients in whom the tubal function was poorer.

This method appears to be ideally suited for measuring the tubal function in patients with chronic secretory otitis media which had necessitated a tubulation of the tympanic membrane by the method of Armstrong (1954).

The examination was conducted as follows: Pressures were applied by means of the Madsen ZO 70 impedance apparatus, which contains a pump system and will register pressures within a range of ± 400 mm water. Fitting of the insert to the ear canal was performed in the usual way by means of Medrescotype plastic tips. We first applied a slowly increasing positive pressure. Under normal circumstances this will cause an opening of the Eustachian tube in a passive way when a pressure of 250–300 mm water is reached. If no such opening was obtained within the measuring range of 400 mm pressure, the patient was requested to swallow some water in order to provoke an active opening. If the pressure following the opening of the tube did not reach a value close to zero it was attempted to cause a further reduction by repeated swallowing. This procedure served to prove that the drainage tube functioned, and at the same time to measure how large a positive gradient was needed to cause an opening of the tube.

We then proceeded to the application of

harmless condition. The therapeutic procedures which are available and necessary are in general extremely simple.

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DISCUSSION

P Berdal Tuba aperta does not always represent a pathological condition My own tubes have been patulous for more than 20 years without signs other than movements corresponding to the respiratory phases.

O Meurman How many cases with cut trigeminal in the middle ear after such an operation are likely to occur I have seen a case of chronic serous otitis media which developed after operation for trigeminal neuralgia.

K Flisberg (Reply to Berdal) There are probably several individuals who have patulous tubes, either constantly or periodically Some of them do not notice the condition in a more scientific way However some individuals, who are sensitive, really suffer from the symptoms, and this group should obviously be treated. There is another group of individuals who can voluntarily open the Eustachian tube. This capacity is often found among pilots who because of their work are exposed to rapid and great pressure changes and have to learn how to equilibrate

(Reply to Meurman) Among the 90 patients with patulous tube there were five who had been subjected to retrogasserian neurectomy because of trigeminal neuralgia The question whether tuba aperta or tuba clausa (obstructed tube) will develop postoperatively depends on the operative procedure and the part of the trigeminal nerve that has been damaged If the sensory innervation of the lower part of the Eustachian tube is through the trigeminal nerve and the motor innervation to the opening muscles is intact retrogasserian neurectomy may result in atrophy of the mucous membrane with at patulous tube If however the motor innervation to the tensor veli palatini muscle is damaged in the operation, it is possible that this will result in a closed Eustachian tube if the mucous membrane affection does not predominate There are undoubtedly cases with serous otitis or chronic otitis media after this operation

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EUSTACHIAN TUBE PATENCY IN CHRONIC EARS

PRE-OPERATIVE EVALUATION CORRELATED TO POSTOPERATIVE RESULTS

A. Palva and J. Kärjä

From the Department of Otolaryngology, University of Oulu, Finland

Eustachian-tube patency was measured with Bortnick technique in 120 chronic ears. The positive test correlated reasonably well with good postoperative results in the normal tympanum and in cases of mild tympanal pathology. In general, the otomicroscopic result was found to provide a more reliable basis for estimation of the prognosis of tympanoplasty. If the formation of adhesions during the primary healing period is prevented, the function of the Eustachian tube can postoperatively be restored, making an aerated tympanum possible.

Proper function of the Eustachian tube is one of the main requirements for successful tympanic reconstruction, and testing the patency of the tube is at present one of the routine pre-operative examinations. A number of tests have been presented from which quantitative information is gained on the function of the Eustachian tube (Flisberg *et al.*, 1963; Miller, 1965; Bortnick, 1966; Siedentop *et al.*, 1968). Only a few studies (House & Sheehy, 1963; Holmquist, 1968; Siedentop *et al.*, 1968) have dealt with the real significance of pre-operative Eustachian-tube function tests, i.e. with their correlation to postoperative results. Much additional clinical information on this subject is required.

MATERIAL AND METHODS

The series consisted of 120 chronic ears. In 25 cases, simple myringoplasty was performed, the others were subjected to radical mastoidectomy with various types of tympanoplasty (Palva *et al.* 1967; Palva, T. 1968, 1969). The postoperative observation time varies from one to three years. The hearing result was considered successful if the practically useful level 0–40 dB (ISO-standard, Davis & Kranz, 1964) was achieved and maintained.

The pre-operative measurement of Eustachian-tube function was as follows (Bortnick, 1966): the external auditory canal was fitted airtight with a No. 12 Foley catheter connected to a manometer. The pressure in the system could be changed from +30 cm H_2O to −30 cm H_2O. The minimum positive pressure necessary to open the Eustachian tube passively was first measured. Thereafter a negative pressure of −30 cm H_2O was established in the middle ear and the possible equalization of the pressure during ten subsequent swallows was observed. The test was considered to indicate Eustachian-tube patency and thus to be positive if a pressure of 30 cm H_2O or less opened the tube and/or if the decrease in negative pressure after swallowing exceeded 5 cm H_2O.

RESULTS

Myringoplasty

All 25 myringoplasty ears had a dry central perforation. The tympanal mucosa appeared normal when inspected with an otomicroscope. Pre-operative testing of Eustachian-tube function was positive in 17 and negative in eight ears. The results are illustrated in Fig. 1. The single failure in healing, and consequently in hearing gain, was due to postoperative infection.

negative pressures. It was first ascertained if a pressure of − 200 mm would give an opening during swallowing. The examination was repeated with pressures of −300 and −400 mm water

The amount of air that passes through the tube during such an active opening is small and it is important that the total volume of the measuring system is not too large, as otherwise many swallowing actions may be needed to reach the final value In the apparatus used the pump system together with the tubes has a capacity around 1.5 ml which proved to be adequate.

We examined a total of 18 children. Their ages ranged from 3 to 15 years. The proved duration of the condition 2 months to 7 years. The first examination was performed on the first postoperative day and then at regular intervals up to 6 months. The results show rather surprisingly that none of the patients were able to reduce negative pressures at all at any time during the follow up

In the immediate postoperative period 54 % were able to reduce positive pressures to a level of 10 cm water At the end of the follow up, 76 % would achieve this level but here the number of subjects is very small 45 % (11) of the drainage tubes were extruded in the observation period most of them during the fifth or sixth month

In seven patients this necessitated retubulation In three patients, the middle-ear pressure was pathologically negative, but so far without recurrence of secretion One patient did not return for follow-up

Conclusions

The tubal function in a group of patients with chronic secretory otitis media measured according to the aspiration method was very poor The level to which positive pressures could be reduced indicated a tendency to very slight improvement during the observation period but without exceptions the function remained very poor

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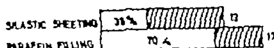


Fig. 3. Results of tympanoplasty in 30 cases of tympanoplasty in ears with diseased tympanic mucosa and negative test of Eustachian-tube function. The cases are related to the method used for preventing tympanal adhesions. The shadowed area indicates failure in tympanoplasty.

membranous scar near the tubal isthmus, each in one case. In 18 cases (31 %) the cause of the negative tubal function test could be found neither on otomicroscopy nor at operation.

In the group of 23 cases with a normal tympanal mucosa, the tympanoplasty was successful in 19 (83 %). The causes of failure were: one serous labyrinthitis pre-operatively, one postoperative infection leading to perforation of the tympanic membrane, one partially adhesive tympanum and one case of deterioration of hearing one year after operation without apparent cause.

When the tympanic mucosa was diseased and the Eustachian-tube function test negative, the tympanoplasty was successful in 17 cases (49 %). Causes of failures were: adhesive tympanum in seven, perforation of the tympanic membrane in six, two of whom showed recurrent discharge. In five cases, no reconstruction was made: two cases had a labyrinthine fistula, and three an extremely severe tympanal pathology.

If the tympanic mucosa had to be removed, the development of an adhesive tympanum was very common if no special method was used for its prevention (Palva *et al.* 1968, Palva, A. 1968). Thus, in the present series, Silastic sheeting or paraffin filling was utilized in 30 cases. Fig. 3 shows the results of tympanoplasty in cases of diseased tympanic mucosa with negative result in the Eustachian-tube function test, as related to the method used for prevention of adhesions. It is seen that, using a careful operation technique and an appropriate method, the development of an adhesive tympanum can be noticeably reduced. This finding indicates the restoration of Eustachian-tube function after healing of infection.

DISCUSSION

A positive Eustachian-tube function test correlates best with the postoperative results in cases of normal tympanum or of mild tympanal pathology. However, an otomicroscopic examination clearly gives more reliable information on the success of a future tympanoplasty. This fact is seen from Fig. 2, in which the cases with normal tympanic mucosa were equally successful (77 % and 83 %) in spite of differences in the Eustachian-tube function tests. The same applies to the myringoplasty cases. Thus, we wish to stress the statement of House & Sheehy (1963) that it is the otomicroscopic evaluation that tells us much about the Eustachian-tube function in most cases.

There are various causes of failure of tympanoplasty. The most uniform group is the development of an adhesive tympanum, which may often suggest hypofunction of the Eustachian-tube. However, a very important part is played by the adhesions forming between the reconstructed tympanic membrane and the bare promontory bone during the immediate postoperative period in spite of Valsalva manoevring and Politzeration. This is clearly evident from our previous experience (Palva *et al.* 1968, Palva, A. 1968, Palva, T. 1969) and also from Fig. 3. Similarly, a situation familiar to every operating otologist can appear postoperatively later on: some months after tympanoplasty the posterior part of the tympanum is adhesive, while in the anterior corner an aerated small tympanum may be discovered as evidence of the restoration of Eustachian-tube function. If the development of adhesions can be effectively controlled during the healing period, the restoration of Eustachian-tube function permits adequate ventilation of an open tympanal cavity.

In the light of these facts we cannot agree with the statement that a negative result in testing for Eustachian-tube function is a con-

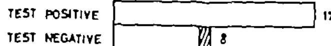


Fig 1 Results of pre-operative Eustachian tube function tests and tympanoplasty in 25 cases of myringoplasty The shadowed area indicates failure in tympanoplasty

Radical Mastoidectomy

For examination of the results of tympanoplasty in these patients the condition of the tympanal mucosa must be evaluated We have classified the patients as follows those having a normal or moderately thickened mucosa and those in whom the mucosa was granulating contained squamous epithelium or was otherwise in a condition necessitating removal

Eustachian Tube Function Test Positive

A positive Eustachian tube function test was found in 37 (39 %) of the 95 ears with radical mastoidectomy in 22 of these for both positive and negative pressure. In 11 ears, patency was obtained only with negative pressure in four cases, the negative pressure showed no tendency to equalization although the positive pressure test opened the tube

Fig. 2 shows in its upper part the 37 cases with a positive Eustachian tube function test related to the state of the tympanal mucosa The majority of cases in this group (31) had normal tympanic mucosa. In seven of these ears (23 %) tympanoplasty was not successful the causes of failure being otosclerotic stapes fixation in two labyrinthine fistula in two on whom no tympanoplasty was performed

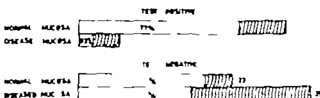


Fig 2. Results of pre-operative Eustachian-tube function test and tympanoplasty in 95 cases of radical mastoidectomy The cases are grouped according to the state of the tympanal mucosa The shadowed area indicates failure in tympanoplasty

and the development of an adhesive tympanum in three

Among six patients in whom the tympanic mucosa was diseased there were four failures: one tympanosclerotic fixation of the ossicular chain one malposition of the prosthesis in an aerated tympanum one labyrinthine fistula with no ossicular reconstruction and one postoperative development of adhesive tympanum Thus, of the 11 failures in this group, four were caused by the development of an adhesive tympanum In two of these the Eustachian tube did not open at a positive pressure while with negative pressure the equalization was not complete. The other two ears showed a completely positive test, one of these being a case of diseased mucosa. A sign of relatively slight tympanal pathology in these cases with positive Eustachian tube function test was that the ossicular chain was intact in nine cases (24 %) and the stapedial crura were missing in only seven cases (19 %)

Eustachian-Tube Function Test Negative

The test for Eustachian tube function was negative in 58 cases (61 %) These are analysed according to the state of the tympanal mucosa in the lower part of Fig 2 The majority of cases (35 or 60 %) in this category showed a grossly diseased middle-ear mucosa. The severity of tympanal pathology is also indicated by the fact that there were only nine cases (15 %) with an intact ossicular chain, and in 20 cases (35 %) the stapedial crura were absent.

The cause of the negative test result was discovered on otomicroscopy in 40 cases (69 %) In 11 the perforation opened into a cholesteatoma sac, and there was no connection from the ear canal to the tympanum, while the possible existence of an aerated tympanum could be assumed on inspection with the pneumatic speculum In 14 cases, granulation tissue occluded the tubal ostium 10 ears showed a clearly adhesive tympanum and two a bony occlusion Additional causes were a metallic foreign body a tympan[illegible]

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CHRONIC OBSTRUCTION OF THE EUSTACHIAN TUBE TREATED WITH A TYMPANO-MAXILLARY SHUNT

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Four patients with complete obstruction of the Eustachian tube were treated by the application of a shunt between the middle ear and the maxillary sinus with preservation of an intact tympanic membrane Good aeration of the middle ear and improved hearing were obtained in all patients No complications have occurred, but one patient has autophonia. Slipping of the tube in one patient necessitated re-operation. Pressure recordings performed from 2 months to 2½ years postoperatively showed that air was passing up to the middle ear on forced breathing or the Valsalva manoeuvre in all patients.

One problem in middle-ear surgery which has not yet been solved is the management of an obstruction of the Eustachian tube, where the only technique currently available is to fenestrate the tympanic membrane either through an indwelling tube or a natural perforation (Armstrong, 1954 Austin, 1969)

A new method for restoring the ventilation of the middle ear in cases with chronic obstruction of the Eustachian tube has been developed and tested over a period of 2½ years (Drettner and Ekvall, 1967 1969).

METHOD

The principle in this method is to create a permanent communication between the middle ear and the maxillary sinus by means of a silicone rubber tube. The tympano-maxillary shunt (TMS) runs from the anterior part of the middle ear in a groove in the bony meatus under the meatal skin and curves anteriorly in the lateral part of the meatus, to pass above and medial to the zygomatic root and medial to the muscular process of the mandible to the postero-lateral wall of the maxillary sinus, which it enters through a hole.

The silicone rubber tube, which is flexible and radio-opaque, has an internal diameter of 1.2 mm and an external diameter of 2.5 mm. It has several small side holes at the end, which is introduced into the maxillary sinus. It is the same tube which has been employed for many years by neurosurgeons in shunt operations for hydrocephalus. When used in the latter operations, the extreme tip of the tube is closed, but for tympano-maxillary shunts this tip is usually cut.

The TMS is applied under general anaesthesia. A retro-auricular incision is extended along the antero-superior attachment of the pinna. The meatal skin and the annulus fibrosus are elevated from the bony canal, exposing the posterior superior and anterior parts of the middle ear The tympanic membrane is also elevated from the malleus, but is still attached to the umbo The anterior ligament of the malleus is cut. A groove is drilled in the anterior part of the bony meatus from the middle ear out to the medial aspect of the zygomatic root, and the capsule of the temporo-mandibular joint is exposed. A blunt elevator is introduced medial to the zygoma towards the postero-lateral wall of the maxillary sinus pointing to the midline of the incisors of the upper jaw

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tra indication to tympanoplasty The reason for failure, in very many cases, lies elsewhere than in the hypofunction of the Eustachian tube. For a successful tympanoplasty the most important points are the state of the tympanum as evaluated with the otomicroscope and appropriate measures in ossiculoplasty and in the prevention of adhesions

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tube was left in place for one month and used for inflation of the middle ear. All patients had complete obstruction of the Eustachian tube as determined by objective tests of the tubal function also during Valsalva and Politzer manoeuvres, and pressures up to 60 cm H_2O in the nasopharynx did not overcome the resistance.

Transudate was present in the middle ear in all cases at operation. The patient who had had an adhesive tympanic membrane treated with lysis and silastic sheeting during a previous operation, had no adhesions in the middle ear at the application of the shunt, but the tympanic orifice of the Eustachian tube was anatomically completely obstructed.

There were no complications during the operations and healing was excellent (Table 2). The tympanic membranes remained intact. The meatal skin became closely attached to the tube. None of the patients has had acute otitis or sinusitis since the operation. The observation periods since the application of TMS are now from 4 months to 2 ½ years.

The aeration of the middle ears has been excellent except in one patient, in whom there was a recurrence of transudate after 4 months due to slipping of the tube outside the middle ear cavity but it still lay under the meatal skin. No suture to the temporo-mandibular joint capsule had been used in this patient, who was subjected to re-operation 11 months after the first application of TMS, and the tube, which was still patent, was only pushed a few millimetres down in the middle ear and sutured to the joint capsule.

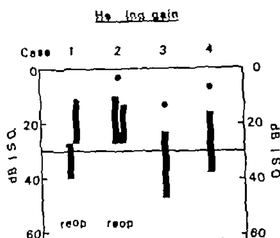


Fig. 1. Hearing results in four patients treated with application of tympano-maxillary shunt.

Re-operation was also performed in the patient first operated on, because of fixation of the incus to the lateral attic wall, already observed during the application of the TMS. A transposition of the incus was performed at this re-operation. There was no transudate in the middle ear and the shunt, which was patent, was left undisturbed.

One patient has some discomfort from autophonia, she hears her own voice as an echo in the treated ear. Another patient has visible movements of the tympanic membrane during respiration as in cases with a patulous tube, but she does not notice it, and she has no discomfort.

Table 2. *Results of TMS*

Case No.	Healing	Aeration of middle ear	Discomforts	Re-operation	Observation during re-operation
1	+	+	(Incompletely restored hearing)	Transposition of incus	No transudate TMS in place
2	+	+/−/+	Recurrence of transudate due to slipping of TMS	Repositioning of TMS tube	Transudate Patent TMS tube
3	+	+	Autophonia	–	–
4	+	+	0	–	–

Table 1 *Case reports*

Case No.	Age, in years	Treatment before TMS	Tubal function before TMS	Time of appl of TMS	Observations during op.
1	47	Mod. rad. op + obliteration Middle-ear tube 9 mos.	0	Jan. 1967	Transudate
2	15	Adenoidectomy Repeated myringotomy Middle-ear tube 1 mo.	0	Oct. 1967 (+mastoidectomy)	Transudate
3	36	Mastoidectomy Lysis + silastic sheeting + myringo-plasty + tube in ET 1 mo. Middle-ear tube 6 mos. Cortisone	0	March 1969	Transudate. No adhesions. Anatomical obstr of ET
4	15	Masteoidectomy Middle-ear tube 14 mos. Cortisone	0	March 1969	Transudate

The elevator is then exchanged for a large trochar which has been blunted at the tip Blunt instruments are used in order to avoid injury to the maxillary artery or its branches. The postero-lateral wall of the maxillary sinus can mostly be penetrated with this blunt tro-char The penetration is otherwise performed after changing the blunt mandrin for a sharp-pointed one with the cannula left in situ The mandrin is removed and the silicone tube is introduced through the cannula into the maxil lary sinus The length of the tube inside the maxillary sinus is 2–3 cm The cannula is then removed The position of the tube is checked by aspiration of air and by instillation of Rin ger s solution through the tube, watching for the appearance of the solution from the nasal opening when the head of the patient is turned with the face downwards The tube is cut obliquely at the end entering the middle ear and the length is adjusted so that the tube reaches about 3 mm below the level of the anterior ligament of the malleus. The tube is fixed with a silk suture to the capsule of the temporo-mandibular joint. The auditory mea-tus is then packed and the incision sutured

From the third postoperative day the mid dle ear is inflated daily through the shunt by Valsalva and Politzer manoeuvres. My ringotomy with aspiration of transudate is usually required after one week or more.

The position of the tube can be checked by X ray

The application of TMS can be combined with mastoidectomy and with lysis of adhesions in the middle ear Myringoplasty for small perforations may be performed simultaneously

RESULTS

Four patients have been operated on accord-ing to the method described (Table 1) Their ages ranged from 15 to 47 years. All patients had been treated vigorously for their obstruc tion of the Eustachian tube before the applica tion of the shunt. All had had an indwelling tube through the drum with temporary recov ery but recurrence was seen in all cases when the tube slipped after various periods of time, and one patient had secretion through the tube Efforts to inflate the middle ear by Valsalva and Politzer manoeuvres and by an Eustachian catheter were unsuccessful Mastoidectomy had been performed in all patients except one, in whom it was done simultaneously with the ap-plication of the tympano-maxillary shunt. One patient, who had an adhesive tympanic mem brane, had previously undergone operation with lysis of adhesions, application of silastic sheeting in the middle ear myringoplasty and introduction of a small silicone tube through the Eustachian tube to the nasal opening this

tube was left in place for one month and used for inflation of the middle ear. All patients had complete obstruction of the Eustachian tube as determined by objective tests of the tubal function also during Valsalva and Politzer manoeuvres, and pressures up to 60 cm H_2O in the nasopharynx did not overcome the resistance.

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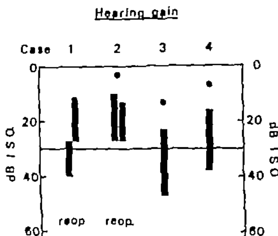


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4	+	+	0	–	–

The hearing improved in all patients, and has remained within the limits of social hearing since the application of TMS (Fig. 1) An auditory regression occurred after the initial improvement in the patient with the slipped tube (case 2) but it was restored after re-operation

FUNCTIONAL STUDIES OF THE TMS

The function of the TMS has been tested by simultaneous pressure recordings from the external auditory meatus after application of a cuff and from the nasal opening while the patient was breathing or performing Valsalva manoeuvres. One patient had movements of the tympanic membrane during respiration an other had very small movements during intense forced breathing. Drum movements were recorded in the other two patients during Valsalva manoeuvres, but not during forced breathing

In order to show that the air was passing through the TMS some special tests have been performed (Drettner & Ekvall 1969) A movement of the tympanic membrane recorded during the Valsalva manoeuvre was lacking when the same manoeuvre as repeated after tamponade of the maxillary ostium. When air was insufflated into the maxillary sinus through a puncture needle while the tamponade was still blocking the maxillary ostium, there was again a movement of the tympanic membrane, showing that air was passing only through the TMS and not through the Eustachian tube Owing to difficulties in obtaining complete blockage of the maxillary ostium, it has only been possible to carry out this test or similar ones in two of the patients. It can *therefore not be proved that air may also pass* through the Eustachian tube in these cases, although that fact that pre-operative tests showed complete obstruction of the Eustachian tube also after treatment with an indwelling tube, and the observation during the operation in one patient that the Eustachian tube was anatomically completely obstructed, favour the opinion that the ventilation occurs *through the* TMS. It is conceivable however that a mucosal swelling in the Eustachian tube may be relieved after treatment with TMS

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EUSTACHIAN TUBE FUNCTION IN TYMPANOPLASTY

CLINICAL ASPECTS

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In order to estimate the significance of pre-operative tests of Eustachian tube function for hearing and healing results, 203 tympanoplasty cases were reviewed. As a routine method Politzer and Valsalva inflations were used as pre-operative tubal tests. Thirty-nine cases were also tested with the aspiration method. Healed drums were found in 79–97 % of the cases (depending on the type of operation). A serviceable hearing (≥ 30 dB I.S.O.) or an air-bone gap less than 10 or 15 dB were achieved in 71–96 % of the cases. Cases with negative aspiration tests did not give inferior results as compared with other cases. The investigation suggests that tympanoplasty should not be regarded as contra-indicated on the basis of pre-operative tubal tests. In manifest postoperative tubal insufficiency a good hearing, even in the presence of a healed drum, may be attained by way of a tubal by-pass (Armstrong tube or tympano-maxillary shunt).

In the pathogenesis of chronic otitis, hypofunction of the Eustachian tube is undoubtedly important. Similarly experimental investigations made by Miller (1965), Flisberg (1966) and Siedentop *et al.* (1968) showed that a very high percentage of cases of chronic otitis have abnormal Eustachian tube function. This abnormality is seen as an inability to equilibrate, by swallowing, a negative pressure in the middle ear applied through the external auditory meatus. The above authors reported Eustachian tube hypofunction in 58–76 % of cases of chronic otitis, recorded by the aspiration method. However the relation of this high incidence of hypofunction of the tube to the results of reconstructive middle-ear surgery and especially to the indications for surgery has been unclear. Some authors consider a recorded hypofunction of the tube as a highly unfavourable prognostic sign in tympanoplasty even contra-indicating reconstructive surgery (Flisberg 1966) Holmquist, 1968). On the other hand, very good healing is reported in large tympanoplasty series without mentioning any tests of tubal function whatsoever (Sheehy & Glasscock, 1967).

In order to find out to what extent this high incidence of Eustachian tube hypofunction in chronic otitis is correlated to healing and hearing, a follow-up study was performed on 203 tympanoplasty cases, operated on between 1963 and 1968. Four cases, operated on during the same period, were not followed up. Three of these died from intercurrent disease and one suffered from severe mental illness.

SURGICAL TECHNIQUE AND POSTOPERATIVE CARE

The surgical technique was almost uniform throughout the series. Tympanic membrane grafting was performed with mesenchymal autograft, vein or temporalis fascia, placed on the medial surface of the perforation. The graft was usually supported by Gelfoam or blood clot in the middle-ear cavity. Even in perforations of moderate size, the whole medial surface of the drum was covered by graft. In cases of large peforations, an extension of fascia (or vein) was inserted between the inner part of the canal skin and the bony meatus to secure an overlap of skin on the graft. Ossiculoplasty when needed, was performed with autografted ossicular remnants, cortical bone or tragal cartilage. In most of the cholesteatoma cases a

closed technique was used Previously operated radical cavities were obliterated with muscle flaps and/or bone chips The ear canal was packed with a "rose bud" pack consisting of strips of surgical rayon filled with a synthetic fibre material ("Tacryl") The pack was left in place for a week and then cortisone antibiotic ear drops were applied locally until complete epithelialization had taken place

As routine methods for checking the tubal patency pre-operatively Politzer and Valsalva inflations were used. Absence of tubal patency in these tests did not contra indicate surgery since the block could be due to changes in the middle ear accessible at the operation e g adhesions or cholesteatoma in the tubal orifice In 39 randomly selected cases the aspiration test of Elsberg *et al* (1963) was performed as well as Politzer and Valsalva inflations.

Postoperatively Eustachian tube function was followed very carefully Returning middle-ear ventilation was experienced by the patient as a popping sound when swallowing If this had not occurred within 8–10 days postoperatively daily Politzer or Valsalva inflations were begun They were continued until spontaneous middle-ear ventilation was able to maintain an air filled tympanum a mobile drum and good hearing. In all cases with larger mucous membrane lesions caused by adhesions, tympanosclerosis or cholesteatoma inflation was started on the third or fourth postoperative day without waiting for signs of spontaneous ventilation. During the first 1–2 months after operation all patients were treated with decongestants in the form of vasoconstrictor nasal drops in alternate weeks and with vasoconstrictor antihistamine oral tablets continuously In addition all patients were instructed to recommence this decongesting therapy prophylactically for 1–2 weeks during every subsequent upper respiratory infection for at least 1–2 years or as long as necessary With impaired hearing following an upper respiratory infection they were instructed to do Valsalva inflations

Table 1 *Distribution of the cases on the basis of pre-operative pathology and type of operation For details see text*

Type of operation	No. of cases
Myringoplasty	91
Myringoplasty and ossiculoplasty	35
Primary reconstruction in cholesteatoma	37
Reconstruction in radical cavities	6
Reconstruction in adhesive ears	14
Total	203

MATERIAL

On the basis of the existing pathology and the corresponding type of operation, the 203 cases were divided into five groups (Table 1) The first group myringoplasty comprised ears with drum perforations but with complete ossicular chains, mobile or mobilized at surgery Cases with drum perforation and stapes fixation as the only ossicular lesion were included in this group These latter cases were primarily mobilized or secondarily stapedectomized. The second group comprised ears with perforated drums and interruption of the ossicular chain, necessitating myringoplasty and ossiculoplasty No cases with ossiculoplasty in a pre-operatively closed and ventilated middle ear were included In this group and in the following a division was made into cases with a complete stapes and cases with the footplate as the only remnant of the stapes. The third group consisted of cholesteatoma cases in which primary reconstruction of the middle ear was performed at the same operation In all these cases, the ossicular chain was interrupted pre-operatively or had to be removed at operation. Thus no cases were included in which a pre-operatively functioning middle ear could be preserved i e cases of conservative radical operation. A closed technique or obliterative procedure was used in 33 of the 37 cases in this group. The reconstructed radical cavities consisted of cases with absent or severely damaged ossicular chains. Cases with partially

Table 2. The 39 cases in which aspiration tests was performed distributed by type of lesion and type of Eustachian tube function according to Miller (1966)

	Miller type				
Type of lesion	I	II	III	IV(V)	Total
Perforation	1	5	2	13	21
Perforation and ossicular lesion	–	2	1	4	7
Cholesteatoma	1	–	1	1	3
Radical cavity		2	1	2	7
Adhesive ear		–	–	1	1
Total	4	9	5	21	39

preserved middle ears were included in the first two groups. All of the 26 radical cavities were obliterated. The 14 cases of adhesive middle ears had total or subtotal obliteration of the tympanic cavity with loss of the mucous membrane. In most of the cases, the ossicular chain was absent or seriously damaged. "Silastic" sheeting was used in some of the cases to prevent recurrent adhesions.

The 39 cases with quantitative tubal test (*aspiration method*) are shown in Table 2. The test was performed according to Flisberg *et al.* (1963) with some modifications. With the patient in the sitting position, a step-wise increasing negative pressure was applied to the middle ear through the external auditory meatus. Pressures of − 20, − 50 − 100 − 200 300 − 400 and − 500 mm of water were used. Equilibration followed every level of negative pressure. For each level the patient had to swallow (by drinking water) at least 10 times during 1 minute and pressure changes in the external auditory meatus were recorded. Each test was followed by recorded Politzer and Valsalva inflations. The results are grouped according to Miller (1965), on the basis of the remaining negative pressure which the patient is unable to equilibrate by further swallowing. No positive pressure was used, so that possible cases of type V according to Miller with complete inability to equilibrate either positive or negative middle-ear pressures, were put down as group IV. The distribution of the 39 cases with aspiration test in regard to pathology and type of operation was similar to that of the main series. Of the cases, 54 % were unable to equilibrate a negative pressure applied to the middle ear and this figure accords fairly well with the corresponding percentages reported in large series by Miller (51 %) Flisberg (58 %) and recently Siedentop *et al* (65 %) There seemed to be no definite difference in type of tubal function among the various types of lesion. One of the cholesteatoma cases and four of the radical cavities displayed surprisingly good tubal function.

RESULTS

All ears were examined by an independent observer as well as by the surgeon. Otomicroscopy and pure-tone audiometry were carried out. Information regarding transient hearing impairment during upper respiratory infections was recorded, in order to estimate the postoperative frequency of a relative tubal insufficiency. Healing and hearing results are shown in Figs. 1–5. Pre- and postoperative hearing (in dB I.S.O.) are given as means of the frequencies 500, 1000 and 2000 cps. Filled bars indicate hearing improvement, unfilled hearing impairment. Postoperative bone conduction level is indicated by a horizontal line. In the various groups, the cases are arranged in chronological order from the left and the time of observation is given at the bottom. The shortest time of observation is 6 months. Cases subjected to re-operation are marked with *reop*

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ostrong e	TMS	Serviceable hearing (≥ 30 dB I.S.O.) or air-bone gap within	Acute serous otitis in upper respiratory infection	Acute otitis media
	–	10 dB 87 (96 %)	40 (44 %)	3 (3 %)
	–	10 dB 32 (91 %)	15 (43 %)	3 (9 %)
3 %)	1	10 dB 31 (84 %)	15 (41 %)	3 (8 %)
	–	*15 dB* 19 (73 %)	11 (42 %)	–
(7 %)	1	15 dB 10 (71 %)	4 (29 %)	1 (7 %)

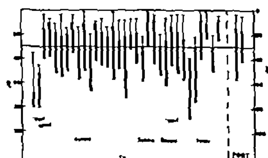


Fig. 2. Hearing and healing results in 35 cases in which myringoplasty and ossiculoplasty were performed. For details, see text.

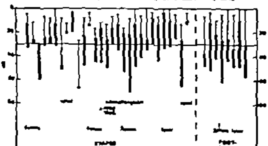


Fig. 3. Hearing and healing results in 37 cases of primary reconstruction following removal of cholesteatoma. TMS tympano-maxillary shunt. For details, see text.

by a permanently implanted silicon rubber tube, a tympanomaxillary *shunt (TMS)* (Drettner & Ekvall, 1967 1969)

The results of surgery in the five groups are summarized in Table 3 which also demonstrates the frequency of postoperative acute serous otitis, diagnosed from hearing loss *during* upper respiratory infection. In 10 patients, acute otitis media developed once or repeatedly post operatively usually with spontaneous perforation of the drum. Nine of them healed with hearing restored, but in one case there is still a small perforation. In the first three groups (myringoplasty *myringoplasty* and ossiculoplasty primary reconstruction in cholesteatoma) the hearing result was considered satisfactory if the 30 dB level was reached, or if the air-bone gap was closed within 10 dB. In the

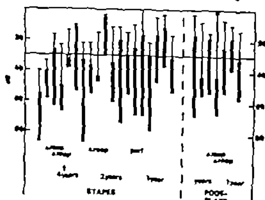


Fig. 4. Hearing and healing results in 26 cases of reconstruction in radical cavities. For details, see text.

other two groups (radical cavities and adhesive ears) a postoperative air-bone gap within 15 dB was considered acceptable.

Table 3 *Healing and hearing results in the 203 cases according to type of operation and incidence of acute serous otitis and acute otitis media postoperatively For details see text*

Type of operation	No. of cases	Healed drum	Perforation
Myringoplasty	91	88 (97 %)	3 (3 %)
Myringoplasty and ossiculoplasty	35	3[illegible] (91 %)	3 (9 %)
Primary reconstruction in cholesteatoma	37	34 (92 %)	[illegible] (5 %)
Reconstruction in radical cavities	26	25 (96 %)	1 (4 %)
Reconstruction in adhesive ears	14	11 (79 %)	(14 %)

and in these cases the primary hearing result is indicated by an interruption in the filled bar Eleven ears had perforations, and nine of these had been noticed within 6 months post operatively

On account of postoperative chronic serous otitis two cases were treated with Armstrong tubes (Armstrong, 1954) In two other cases with the same problem the middle ear and the maxillary sinus of the same side were connected

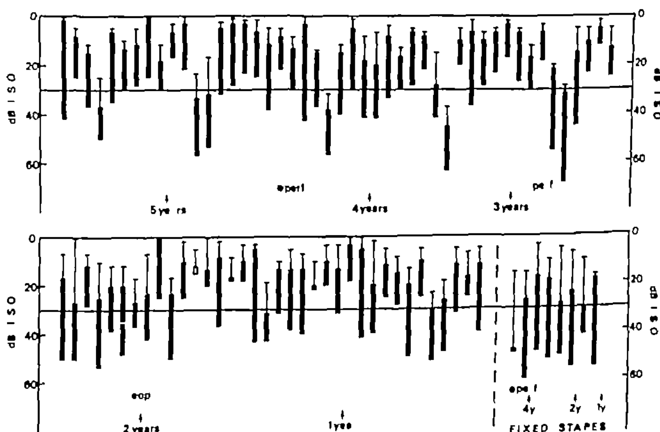


Fig. 1 Hearing and healing results in 91 cases in which myringoplasty was performed *perf* postoperative perforation *reop* = re-operation (incomplete hearing due to separation of the drum from the handle of the malleus no perforation existed). For details, see text.

Armstrong tube	TMS	Serviceable hearing (≥ 30 dB I.S.O.) or air-bone gap within	Acute serous otitis in upper respiratory infection	Acute otitis media
		10 dB 87 (96 %)	40 (44 %)	3 (3 %)
		10 dB 32 (91 %)	15 (43 %)	3 (9 %)
1 (3 %)	1	10 dB 31 (84 %)	15 (41 %)	3 (8 %)
		15 dB 19 (73 %)	11 (42 %)	–
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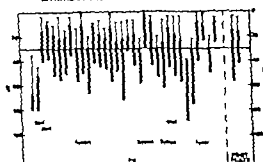


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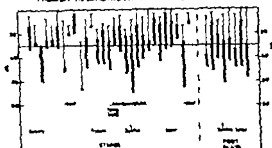


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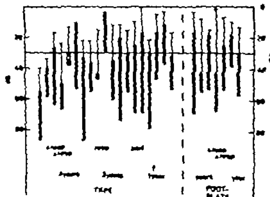


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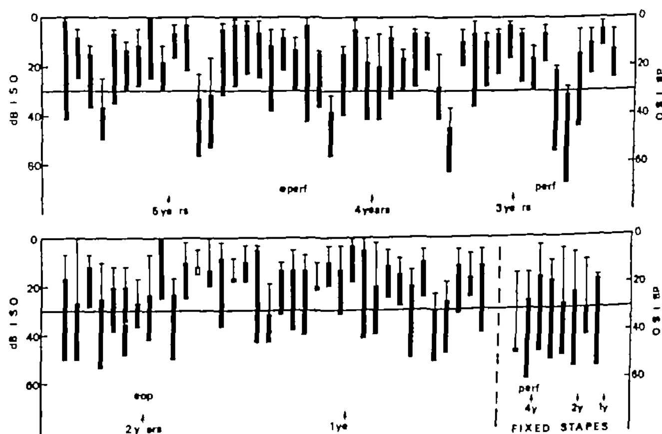


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only way of middle-ear aeration in these patients, but it should prevent locking of the tube and thus permit some spontaneous ventilation.

In spite of very careful decongesting prophylaxis in common colds and acute rhinitis, a high and strikingly constant frequency of acute serous otitis exists in the various groups. In the cases with a negative aspiration test, this frequency is even higher as might be expected. The high incidence of acute serous otitis postoperatively suggests that a relative hypofunction of the Eustachian tube often exists, even after a successful tympanoplasty. This finding is in accordance with those of Siedentop *et al.* (1968) in pre- and postoperative aspiration tests in 25 cases.

The only one of the 21 cases in the group of negative aspiration test that has not reached the 30 dB level has a well-ventilated middle ear and the reason for the remaining air-bone gap is certainly an ossicular problem. The findings in this group suggest that a negative aspiration test does not exclude a good hearing result in the presence of a healed drum. This, too corresponds with the observations made by Siedentop *et al.*, viz. that, in most cases it is not possible to predict the surgical result on the basis of pre-operative Eustachian tube function. Even a negative result of patency tests in the form of Valsalva or Politzer inflations, or tubal catheterization, should not contra-indicate tympanoplasty as the cause of the block might be adhesive lesions closing the middle-ear orifice of the tube (Zöllner 1963).

In adhesive middle ears there has been some doubt as to whether the Eustachian tube is anatomically open. However clinical observations under the otomicroscope very often disclose an air-filled and closed cavity in the tubal orifice which is conclusive of a functioning Eustachian tube (Wullstein, 1960). This feature could not be demonstrated pre-operatively in eight of the 14 cases of adhesive middle ears in the present series. However in not less than seven of these eight cases which presented as totally obliterated middle ears at operation, was an air-filled cavity lined with normal mucous membrane found in the bony portion of the tube. Neither an aspiration test, nor inflation with any of the available methods would have revealed the ventilating capacity of the tube in these cases. In only one of the 14 adhesive middle ears was an anatomical tubal closure found. The findings in this group suggest that a functioning Eustachian tube often exists, even in adhesive ears, and that the main surgical problem may not be tubal insufficiency but the strong tendency to recurrence of the adhesive lesions per se. Middle-ear implants like "Silastic" sheeting could help in the solution of this problem.

The four cases with postoperative chronic serous otitis all reached the 30 dB level after inserting the Armstrong tube or the tympanomaxillary shunt. One of the cases (adhesive ear) had an anatomical tubal closure, and this ear is now well ventilated behind a healed drum via the TMS. Thus, if the tubal function is insufficient postoperatively in spite of active tubal treatment, it is possible to attain good hearing by a tubal by-pass. However the prerequisite is that other parts of the middle ear such as the ossicular chain, have been reconstructed. Finally it is of interest to analyse the hearing results in the 11 cases with postoperative perforation, assuming that all these would be caused by tubal insufficiency. Thus, eight of the 11 cases reached the 30 dB level or closed the air-bone gap within 10 or 15 dB. In no case did the hearing deteriorate.

The present investigation suggests that tympanoplasty should not be regarded as contraindicated on the basis of the result of pre-operative tubal tests. In spite of a high postoperative incidence of relative tubal insufficiency it should be possible to achieve a healed drum and good hearing in a comparatively high percentage of operated cases. In manifest postoperative tubal insufficiency good hearing even in the presence of a healed drum, may be attained by means of a tubal by-pass. Failures should primarily be ascribed to incomplete surgical technique or inadequate postoperative care.

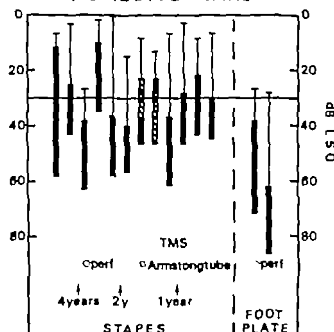


Fig. 5 Hearing and healing results in 14 cases of reconstruction in adhesive ears. Hatched bars indicate the hearing after insertion of the Armstrong tube and the TMS. For details, see text

Among the cases with pre-operative aspiration test, special attention was given to those with complete inability to equilibrate the negative pressure in the middle ear by swallowing (Miller type IV (V) cases) The distribution of these 21 patients in respect to type of operation and the postoperative results are given in Fig. 6 and Table 4 The re-operated case was tested between the two operations. One

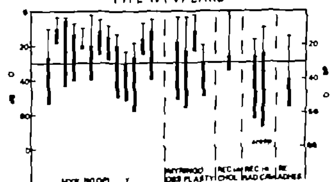


Fig. 6. Hearing and healing results in I cases in which pre-operative aspiration test was negative. For details, see text.

Table 4 *Healing and hearing results and pos[t]-operative incidence of acute serous otitis a[nd] acute otitis media in 21 cases with negati[ve] aspiration test*

No. of cases	21
Healed drum	21 (100 %
Perforation	–
Serviceable hearing (≥ 30 dB LS.O) or air-bone gap ≤ 10 dB or ≤ 15 dB	0 (95 %)
Acute serous otitis in upper respiratory infection	11 (5 %)
Acute otitis media	–

case had not reached the 30 dB level, but th[e] middle ear was well ventilated behind a heal[ed] drum and the remaining air bone gap w[as] certainly due to a refixation of the stapes, whic[h] was mobilized at surgery

DISCUSSION

The surgical technique used permits a ve[ry] early postoperative ventilation of the midd[le] ear by Valsalva or Politzer inflations witho[ut] risk of dislocation of the tympanic membran[e] graft, which is placed on the medial surfac[e] of the drum remnant Many authors have re[-]garded this early ventilation as extremely im[-]portant in diminishing the risk of postoperativ[e] adhesions and atelectasis of the middle ea[r] (Wullstein, 1960 House 1960 Zöllner 1963[)]. An early and regular ventilation *during th[e]* postoperative period will prevent a long-stand[-]ing negative pressure in the middle ear Such [a] negative pressure tends to increase the inevi[t]able postoperative oedema of the mucous mem[-]brane caused by the surgical trauma. The tub[e] could then be locked and a vicious circle en[-]sues. The patient himself can very easily con[-]tinue regular Valsalva inflations until a well ventilated middle ear and good hearing ar[e] established. In exceptional cases, permanent re[-]gular inflations have been necessary to pre[-]serve a good hearing. These Valsalva or Po[-]litzer inflations carried out by the patient him[-]self two or three times a day may not be th[e]

Table 1 *Relation between pre-operative tubal function, postoperative social hearing and recurrent perforation. Relation between pre-operative and postoperative tubal function.*

Pre-operative tubal function	Total	Social hearing		Recurrent perforation	Not passable in Valsalva's manoeuvre postoperatively
Passable in Valsalva's manoeuvre	44	33	75 %	3	2
Not passable in Valsalva's, but in Politzer's manoeuvre or to catheter	16	9	56 %		5
Stenosis to catheter or Politzer	8	6	75 %	1	3
N data	9	7	78 %	4	2
Total	77	55	71.5 %	10 13 %	12

series and by only 58 % of the patients with poor tubal function.

The follow-up comprised 72 out of the 77 patients. The average follow-up period is 18 months, maximum 4 years. Tubal function was assessed by means of Valsalva's manoeuvre (Table 3). Out of the 65 patients who had had a passable tube in Valsalva's manoeuvre 2–3 months after the operation only 48 had so at follow-up. The results in these patients were still as good as after the operation, social hearing being found in 73 % of the cases. On the other hand, 14 patients did not have a passable tube in Valsalva's manoeuvre at follow-up. These patients' hearing had deteriorated somewhat, only 57 % having social hearing as compared with 75 % 2–3 months after the operation.

At follow-up, social hearing was found in 67 % of the total series, i. e. a slightly poorer result as compared with the findings 2–3 months after the operation. This deterioration occurred in the very patients whose tubal function had become worse after the completion of treatment. This indicates the necessity of the patients themselves performing the Valsalva manoeuvre. Out of the 12 patients who had had a non-passable tube in Valsalva's manoeuvre 2–3 months after the tympanoplasty seven again showed patency at follow-up (Table 3). Nevertheless, their hearing had not improved appreciably and the damage caused by the reduced tubal passage after the operation had thus not been materially improved.

The present series demonstrates that tubal function is often somewhat impaired in patients with chronic otitis or the sequelae thereof. Tubal function fluctuates a great deal, and it was not always in the same patients that tubal passage was reduced before the operation, after the operation, and at follow-up. True, the functional results are poorer in patients with

Table 2. *Results 2–3 months after tympanoplasty in 12 patients whose Eustachian tube was not passable in Valsalva's manoeuvre compared with the total series (frequency group 500–2000 cps.).*

			Entire series
Social hearing (0–30 dB.)	6	50 %	71 %
Bone-air gap (0–15 dB.)	3	25 %	56 %
Hearing improvement more than 10 dB.	6	50 %	8 %
TI[1] (0–35 dB.)	9	75 %	86 %
Recurrent perforation	4	33 %	13 %

1 Threshold of intensity

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M Tos

Tubal Function and Tympanoplasty

In Glostrup Hospital Copenhagen, tubal function before and after tympanoplasty has been assessed by the Valsalva manoeuvre Tympanoplastics of types I II and III a total of 77 were performed on patients with sequelae of otitis and perforation of the drum but without discharge. The series is unselected, the operations having been performed also upon patients who pre-operatively had considerably impaired tubal function in the hope of improving it. During the operation the tympanic orifice of the tube was inspected any pathological changes removed, and bougienage was done using a 0 5–1 0 mm rubber bougie which always passed down into the rhinopharynx One week after the operation *the patients started doing the Valsalva* manoeuvre twice daily In the event of reduced tubal passage, Politzer's manoeuvre was done and air was insufflated through a tubal catheter up to twice weekly for two or three months after the operation.

Prior to the operation the Eustachian tube was passable in Valsalva's manoeuvre in 44 cases (Table 1) 2–3 months after the operation 75 % of these patients had social hearing (30 dB or better to frequencies 500–2000 cps.) In 24 patients, the tube was not passable in Valsalva's manoeuvre, and eight even showed distinct stenosis of the tube in Politzer's manoeuvre or in insufflation of air by tubal catheter However 15 (63 %) of these patients obtained social hearing, indicating that impaired tubal function does not contra-indicate tympanoplasty Comparison of tubal function before and after the operation showed that the tubal passage had been improved since after the operation only 12 patients had a non-patent tube in Valsalva's manoeuvre. Out of the 24 patients who had impaired tubal passage in Valsalva's manoeuvre prior to the operation only eight had impaired tubal passage after the operation.

Tubal function during the postoperative period is of great importance for the result. It will be seen that in the 12 patients who had reduced tubal function postoperatively the results are considerably poorer than in the total series, regardless of the criteria by which they are assessed (Table 2) Social hearing was obtained in 71 % of the entire series, but only in 50 % of the patients with poor tubal passage Closure of a bone-air gap up to 15 dB. was obtained in 56 % of the total series, but in only 25 % of the patients with reduced tubal passage A hearing improvement exceeding 10 dB was obtained by 82 % of the entire series, by only 50 % of the patients with a poor tubal passage Recurrent perforations occurred in 13 % of the entire series, in 33 % of the patients with a poor tubal function Social hearing or closure of a bone-air gap of up to 15 dB was obtained by 84 % of the entire

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THREE MODELS FOR TEACHING OTONEUROLOGY

N G Henriksson, C. F Claussen and L. Tibbling

From the Department of Otolaryngology University Hospital, Lund Sweden

Two otolith receptors in each vestibular labyrinth record linear accelerations and three ampullar receptors record angular accelerations.

1 *Rotating otolith model*

Purpose: To show that the otolith receptor is inadequate for recording angular movements as the hair of the receptor bends differently at the same angular acceleration if at different distances from the axis of rotation.

2. *Rotating model of a semicircular canal receptor*

Purpose: To show

A. Cupular deflexion is dependent upon angular acceleration and not upon angular velocity

B This deflexion is independent upon the distance between receptor and axis of rotation.

3 *Model showing transmission of sound-pressure from meatus to inner ear*

Purpose: To show gain in transmission from tympanic membrane to oval window



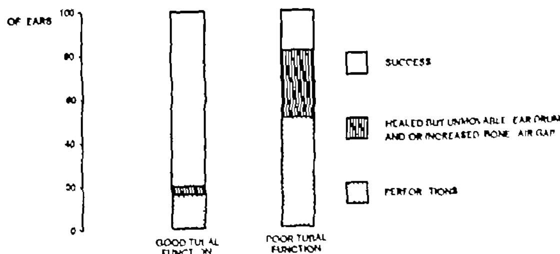
Fig. 1 Otolith model made of plastic (sensory cells forming the macula), steel (sensory hairs) and silver (otoliths). The model is mounted on small rotation table. One of the "cells" can easily be loosened for demonstration of bending of the hair at tilting (½).

Table 3 *Tubal passage in Valsalva's manoeuvre 2–3 months after tympanoplasty compared with the tubal passage 18 months after the operation*
Relation between tubal function and social hearing

Valsalva's manoeuvre 2–3 months after the operation				Valsalva's manoeuvre 18 months after the operation					
		Social hearing		Passable	Social hearing		Not passable	Social hearing	
Passable	65	49	75 %	48	35	73 %	14	8	57 %
Not passable	12	6	50 %	7	4	57 %	3	1	33 %
Total	77	55	71 %	55	39	71 %	17	9	53 %

reduced tubal function, but nevertheless the series includes many cases in which the hearing was improved sufficiently to be designated social hearing. The poorest results were seen in cases in which tubal passage had been reduced postoperatively. Therefore, intensive insufflation of air is necessary soon after tympanoplasty.

J. Holmquist: Adequate tubal function is a prerequisite for success in tympanoplasty. However, when the surgical procedure includes restoration of tubal function, ears with poor function of the tube may also be subjected to operation. This figure shows 2 year follow up results after myringoplasty in 94 years. The operative procedure included only covering of the eardrum defect by fascia after de-epithelization of the drum remnant. Ears with "good" tubal function (according to the aspiration method and equalization into the range of 0–100 mm water) healed in 80 % but only 20 % of the ears with "poor" function healed satisfactorily. This means that the pre-operative tubal function test is able to give prognostic evidence which must not be questioned. However, these results also suggest that the surgical procedure must be focused not only on the eardrum defect, but also on the restoration of the Eustachian-tube function, the middle ear and the mastoid air-cell system.



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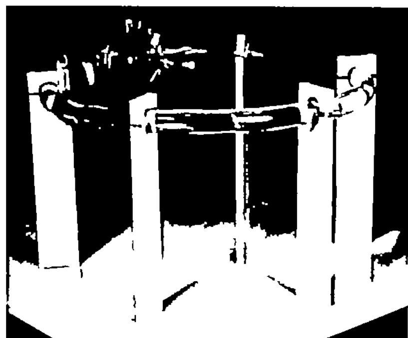


Fig — Model of semicircular canal system. Canals of glass, cupula of specially made plastic. The model is mounted on a small rotation table for demonstration of per and post acceleratory bending of the cupula (1/1).

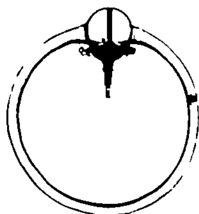


Fig. 3 Model of the middle ear with tympani membrane and inner ear With glass tubes on both sides different pressures can be achieved in the outer meatus and in the inner ear
The tympanic membrane oval and round windows are made of rubber membranes, ossicular chain of glass rods. The loose connections between ossicles are demonstrated by glass coupling (1).

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PHOTOGRAPHY IN TRANSCONIOSCOPY

H Sorensen

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Transconioscopy has proved valuable in many diseases in the larynx. Transconioscopy should especially be used in the topical diagnoses of laryngeal cancer In many cases of glottic cancer the caudal extension of the tumour cannot be determined without transconioscopy Small lesions in the subglottic space that could not be diagnosed by X-ray tomography and direct laryngoscopy have been revealed by transconioscopy

The examination is performed in local anaesthesia as described by Mårtensson.

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VASCULAR ANATOMY OF THE HUMAN TEMPORAL BONE

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Temporal bones were removed from the body and afterwards injected with a coloured medium under controlled physiological pressure Selective injections were performed into the internal auditory or subarcuate artery through the anterior inferior cerebellar artery The specimens were studied by means of microsurgical dissection methods.

The exhibition showed examples of (A) the vascular anatomy of the cerebello-pontine angle and the internal auditory canal (B) vascular anastomoses within the temporal bone

A 1 Various vascular patterns of arteries extending from the basilar artery to the posterior aspect of the temporal pyramid (into the internal auditory canal and the subarcuate fossa)

2 Different configurations of the anterior inferior cerebellar artery loop plus the internal auditory and subarcuate arteries.

3 Course and division of the single or multiple internal auditory artery inside the internal auditory canal

B 1 Interconnections between the internal auditory and subarcuate arteries.

2 Arterio-venous shunts between the subarcuate artery and superior petrosal sinus

3 Anastomoses between the vertebro-basilar system and branches originating from the carotid arterial system at the level of the enchondral bone all around the labyrinth

4 Anastomoses between branches from the internal auditory and subarcuate arteries and those supplying the middle-ear promontory

Comments

The internal auditory and subarcuate arteries are branches from the same arterial loop, which is either the anterior inferior cerebellar artery itself or its collateral branch Two or more internal auditory arteries originated from the loop in about one half of the cases. In the remaining specimens only one such artery was found.

Inside the internal auditory canal, the single internal auditory artery usually runs along the anterior or the anterosuperior aspect of the eighth nerve. When present the second internal auditory artery is usually situated along the postero-inferior aspect of the eighth nerve complex

The subarcuate artery commonly enters the petrous bone at the level of the subarcuate fossa and only rarely through the posterior wall of the internal auditory canal.

A remarkable feature of the peripheral course of both the internal auditory and subarcuate arteries is their distribution to the otic capsule The branches from these arteries not only communicate freely with each other but in bones injected with contrast medium through vessels both from the carotid artery system branches from the carotid and those from the vertebro-basilar system meet in the same vessels all around the labyrinth. The same is true of the vessels on the tympanic promontory The tem

poral bone therefore appears as an area in which branches from the intracranial circulation extensively communicate with branches from the extracranial vascular bed. A better understanding of the functional value of such communications may be of clinical significance.

Finally it should be mentioned that the material injected into the facial nerve sheath from the internal auditory canal side extended as far as beyond the stylomastoid foramen level.

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PHONIATRIC DIAGNOSIS

B Fritzell

From the Division of Phoniatrics Department of Otolaryngology University Hospital Göteborg Sweden

In Scandinavia phoniatrists deal with all kinds of disorders of oral communication Oral communication is behaviour From a medical point of view disturbances in a person's speech, voice and language behaviour are symptoms. Thus, phoniatric diagnosis primarily involves analysis and classification of symptoms. Secondly but medically more important, the phoniatrist must find out what causes the symptoms and deviant behaviour and arrive at an aetiological diagnosis. A number of problems pertain to phoniatric diagnosis, such as definitions of normalcy measuring procedures to determine degrees of abnormalcy and terminology

In Scandinavia, phoniatrists deal with all kinds of voice speech and language disorders. These disorders represent symptoms of a variety of underlying disturbances and diseases which interfere with the normal development of the growing child or with the communicative behaviour of the adult individual, who has well established speech and language patterns. Since the mechanisms of human oral communication are exceedingly complex, the systematic approach to phoniatric diagnosis requires a simplified model to serve as a frame of reference (Fig. 1)

When a speaker wants to communicate a thought to his listener he forms his thought into a code of words and sentences. From his speech motor cortex action potentials representing this code pass through lower levels of the central nervous system and along motor nerves to the vocal tract, where a large number of muscles are activated to transform the signals into sound waves. The sound waves are received by the ear of the listener and the message again transformed into action potentials. These travel along the auditory nerve and central pathways to the auditory cortex and associated areas, where the message is decoded and perceived. In the control of the speaker's output, his hearing and his tactile and kinesthetic proprioception are the necessary feed back mechanisms.

The phoniatrist is confronted with speakers who do not function normally In making his diagnosis, he primarily plays the role of the listener His first task is to analyse the symptoms, i e. the sound waves and the deviant behaviour of the speaker Secondly he seeks to find out what has caused the symptoms, to arrive at an aetiological diagnosis. His diagnostic endeavours also include an evaluation of the prognosis, before the therapeutic programme is made up

Analysis of Symptoms

The analysis of the symptoms is a matter of appraisal and classification of behaviour In clinical practice, this is almost exclusively carried out by *subjective* means, i. e auditorily and visually The examiner listens to the speech and voice of the patient, and he observes the movements of the articulators, the approximation and vibrations of the vocal folds, the respiratory mechanism, etc. He determines in what respect and to what extent the findings deviate from normal behaviour For some speech and language functions standardized test procedures are available, which may be

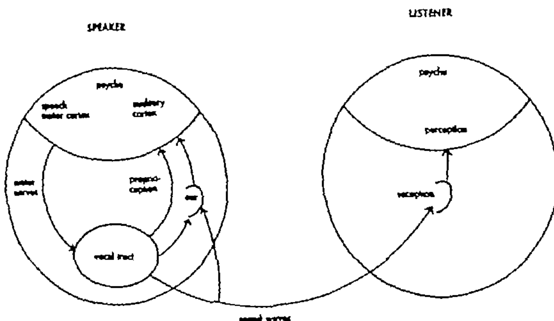


Fig. 1

used to provide measures, and not verbal descriptions only (Johnson *et al.*, 1963)

However as a consequence of the advanced development of medical technology in recent decades, we have very refined procedures at our disposal to record and analyse speech and ocal behaviour *objectively* (van den Berg, 1962) The sound waves emitted by the speaker may be studied in detail by acoustic analysis (Fant, 1960) The flow of air and the air pressure in various parts of the vocal tract may be recorded and measured by aerodynamic procedures (Hardy 1965) The articulatory movements may be subjected to motion-picture analyses, some by regular photography others by X-ray procedures (Moll, 1965) The activity of the muscles involved in speech production may be studied by means of electromyography (Fromkin & Ladefoged, 1966)

Besides these general approaches to the study of the peripheral speech mechanisms, a large number of special techniques may be used in the detailed analysis of respiration, phonation and articulation. Thus, the vibrations of the vocal folds may be recorded *optically* by stroboscopic photography (van den Berg, 1960), high-speed photography (Moore & von Leden, 1956) and photoglottography (Sonesson, 1960), *radiologically* by strobolaminagraphy (Holben, 1965) *electrically* by electroglottography (Fant *et al.*, 1966) and *acoustically* by fundamental frequency analysis (Michel *et al.*, 1966), jitter analysis (Michel *et al.*, 1967), inverse filtering (Lindqvist, 1964) and ultra-sound procedures (Sonesson *et al.* 1969).

Only to a slight extent have these recording procedures been applied in clinical practice. Their use is still mostly limited to the experimental research laboratories. Moreover as research has so far been concerned mainly with normal individuals, very little objective and quantitative information is available on pathological behaviour

One of the main features of behaviour that causes considerable problems in phoniatric diagnosis is the normal variation. Speech and voice characteristics vary considerably from individual to individual. These variations are partly due to anatomical differences, but no doubt also to psychological (Moses, 1954) and other factors, such as age It has been dem-

onstrated that listeners can very accurately tell the age of an unknown speaker simply by listening to his speech and voice from a tape recording (Hollien & Shipp 1967) Speech and voice characteristics also vary considerably within the individual Thus, it is well known that our voice quality changes with our mood. Another source of variation of particular importance in voice diagnosis is introduced by the examiner when he puts his laryngeal mirror in the throat of the subject, who is holding his mouth wide open and extending his tongue How does this affect vocal-fold behaviour?

Consequently we are faced with a great deal of variation This raises the questions What is normal? What is normal variation? Unfortuanately there exists no recognized prototype speaker of Swedish (or any other language) to whom reference can be made, and deviations compared We have to rely entirely upon subjective standards in the appraisal of our patients There is an urgent need for more research on normal variation and for standardized test procedures. Thus, no thorough systematic study of Swedish children's language acquisition has yet been made We do not know definitely at what age our children can be expected to use the correct speech sounds, etc.

Another major problem in phoniatric diagnosis is terminology (Brodnitz, 1967) The way we label the abnormal behaviour of our patients has a great impact on our thinking and handling. But there are very few universally recognized and accepted terms Thus, it is very difficult—if not impossible—to describe verbally the voice characteristics of a patient in such a way that other readers of his record get a clear concept of his voice Nor is there any reliable objective way to measure degrees of dysphonia.

Search for Aetiological Factors

Since therapy must primarily be directed towards the aetiologic factors, the basic and most important task of the phoniatrist is to find out what has caused the symptoms of his patient. A great variety of organic and psychological causes may be responsible Most of the time a combination of factors contributes to the development of a communicative disorder

A very thorough case history is crucial. Whereas the otolaryngologist may often base his diagnosis and therapy on a fairly brief medical case history and on the findings from the visual examination of his patient, the phoniatrist is also highly dependent on information of the social background and setting of his subject, the development of his speech and language behaviour his education and present level of communicative sophistication, the professional environment and demands on his voice, etc. It is necessary to devote much time to the case history and to explore all possible causative factors in depth

In the medical examination of the patient, the psyche the nervous system the vocal tract, and the hearing mechanism are evaluated by routine procedures. It must be emphasized that speech and voice disorders may be symptoms of diseases falling within the realm of many other medical specialties. For this reason, the phoniatrist must have a basic training in related areas, thorough enough to make him capable of diagnosing and handling common disorders within the fields of otorhinolaryngology audiology neurology paediatrics, psychiatry etc., and of making appropriate referrals when necessary

Making the Diagnosis

On the basis of the analysis of the symptoms the communicative disorder is classified and labelled The aetiological factors should also be included in the diagnosis. It is advisable to follow the example of the child psychiatrists by keeping the symptom labels and the underlying causes apart. Thus, in the patient records there is room for two diagnoses, the symptom diagnosis and the assumed aetiologic factors. Examples.

Phonastenia

Vocal profession + acute laryngitis

Delayed speech development
Congenital hearing impairment

Stuttering
Heredity? + psychic trauma + environment

In this way the behavioural problem is given as a head line, and the aetiologic factors are stressed by appearing as subtitles.

Prognostic Evaluation

As part of the diagnostic procedures an attempt is made to assess the prognosis. The examiner determines to what extent present aetiological factors can be influenced or eliminated, and he judges the chances of changing the patient's behaviour by speech and voice therapy. It must be recognized that changing somebody's behaviour is a difficult task. Age and motivation are the main determinants of success. With increasing age, man becomes less flexible: tissues gradually lose their elasticity, motor patterns stiffen, and mentally we become more rigid. Motivation, however, is the most important factor. Without a strong wish to change on the part of the patient and his full co-operation it is very difficult or impossible to influence his behaviour.

CONCLUSIONS

If a comparison is made between otorhinolaryngology and the medical specialties that have grown out of it—audiology and phoniatry—the principal differences may be found in the fact that the otolaryngologist—in his capacity as surgeon—is primarily concerned with structure, the audiologist with perception, and the phoniatrist with behaviour. Phoniatric diagnosis means an analysis of deviant behaviour and a search for aetiological factors. The phoniatrist serves as an integrator between medicine and the linguistic and behavioural sciences.

Phoniatric diagnosis is still to a great extent a subjective affair, where the ear and the eye of the examiner are the most important tools. In the future, these means should be supplemented by an increased use of instrumental recording procedures and objective standards of evaluation.

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PHONIATRIC EXAMINATION TECHNIQUE

N H Buch

From the Phoniatric Laboratory the Department of Otolaryngology University Hospital Copenhagen Denmark

Voice disorders, disarticulations and language disturbances are frontier regions which demand close co-operation between logopaedians technicians and medical specialists. The experience gained in our recently established Phoniatric Laboratory its organization, its tasks and the most important equipment required for diagnostic work are mentioned.

The care of speech defectives in Denmark originates from the deaf mute cause After the preliminary work of pedagogues and physicians, the Government established in April 1898 the Institute for Speech Defectives. The management was then in the hands of the principal of the Royal Institute for Deaf mutes *in Copenhagen the Reverend Frederik Heiberg*, and Dr Holger Mygind, while C. Goos, LL D., managing director was the superintendent.

From the earliest annual reports of the Institute it appears that the medical leader was soon dethroned and was later referred to as the "family" doctor connected with the institution. Probably other tasks in the field of the new medical speciality otorhinolaryngology required such enormous efforts from the persons involved that the administration of the care of speech defectives was subsequently left with the pedagogues.

In recent years, increasing activity among psychologists and speech therapists, particularly in connection with the development of the special instruction in council schools and county colleges, has strongly marked the picture on the teaching, educational and administrative levels. While during the first half of the century the practical work was best done by centralization of the speech institutes, development have now reached a point at which adequate decentralizing is required, but increased activity efficiency technical improvements and sufficient economy in the work will only be achieved however if diagnostic work and the definition of indications are made more rigorous, and co-operation between the groups involved is further developed.

Moreover the medical contribution to the work for speech defectives in Denmark has so far been too sparse Instruction of the doctors has been very limited and lack of final positions *in the sub-speciality has not inspired* young physicians to make this subject their life-work although it covers—like audiology—so many medical and social aspects that we simply cannot leave it.

It is a well known fact that nearly all speech defects are symptoms of a pathological condition of either organic or psychic origin. Hence, a differentiated medical diagnosis, therapy and instructions form the ideal basis for the efforts of the pedagogue Testing and objectively reproducible methods of examination as well as frequent check ups of the patients, must be adapted to a system comprising good co-operation between logopedians and phoniatricians with other medical specialists, dentists, psychologists and technicians. This—and also the purchase of clinically and scientifically useful apparatus—can hardly be established in insolated institutions today but will be practicable in

connection with the county-municipal development, which will, inter alia, result from the coming administration of the hospital system. The Copenhagen Hearing Centre's move to a hospital area (the Bispebjerg Hospital) is also a natural consequence of similar ideas on the future of audiology

On this background we have during the past years planned the establishment of a phoniatric laboratory at Rigshospitalet in order to contribute to improved diagnosis definition of indications and statistics in the field of speech deficiency The necessity of providing our hospitalized and non-hospitalized patients with sufficient speech therapy when they are most in need of it, has been the practical reason why our Laboratory has been functioning as a unit under the Department of Otolaryngology of the University Hospital, Copenhagen, since the 1st November 1968

The work is in the hands of a senior registrar from the department and the speech disorders are further handled by two speech therapists recruited from the State Institute for Speech Defectives. The patient material originates from our own department and its out-patient clinic, the other departments of the hospital, practising otologists and other colleagues among the physicians.

During the first 5 months of the existence of the laboratory 345 new patients were examined. On an average, they consulted the laboratory 3.2 times each. Owing to certain practical conditions the therapist coverage was not at a maximum during the said period, but it did comprise 85 days of therapeutical work altogether During the period, 284 private lessons and 21 classes, consisting, on an average of five laryngectomized subjects were given. The patients had various organic and psychic complaints, but naturally the co-operation with an ear nose and throat department made speech defects and pronunciation errors predominant. Nevertheless, the language disturbances—including aphasia—constituted one sixth of the treated group The lessons were carried out without any waiting time, and only nine patients had not finished their treatment when discharged from hospital. Consequently for geographical reasons, they were referred to local speech therapists all over the country through the Institute for Speech Defectives.

In the diagnostic work, the laboratory has particularly enjoyed the helpful services of the Department of Radiology the Laboratory of Lung Physiology and from special psychiatric, neurological and physiatric examinations. As regards therapy physiotherapy of various kinds has often been an integrating part. Intensive and frequent speech lessons have been given, and out patients have often had tape recordings of speech exercises for home work. Repeated check-up examinations with tape recordings have in addition to the constant co-operation between physician and speech therapist, contributed to the rationalization.

In the development of the new phoniatric laboratory we have tried to procure apparatus for clinical as well as scientific purposes. The rapid development of electronics will in the future give very high priority to co-operation with engineers, technicians and experimenting phoneticians.

So far we have bought tape recorders, frequency meters, intensity meters, a sonograph, a storage oscilloscope and an electro-aerometer and we have also a Timcke stroboscope at our disposal. We have borrowed a mingograph, and we badly want apparatus for pressure measuring, glottography spectrometry etc.

Partly and fully professional tape recorders are today of such a standard that the choice of make is no longer decisive. We, on our part, use recorders from the Akai-Electric Company The recordings are made in a sound-absorbing room, which is also an audiometer room. For scientific purposes, dynamic condensator microphones are necessary The quality of the microphones must be adapted to that of the tape recorder

In the clinic, it is possible to obtain a *rough* evaluation of the average speech *frequency* by using the pitch meter which is incorporated in most stroboscopes. Where the conditions of

frequency are to be reproduced it is necessary to use a frequency meter in addition to the registration apparatus (oscilloscope or mingograph) We use the Danish made "Trans Pitch meter" with two inlets of 5 and 500 ohms with a view to the balance of impedance Furthermore there are two outputs, as the basic frequency is measurable by simple filtration through five low pass filters, which can be variably inserted depending on the nature of the voice examined. For removal of hum and noise two high pass filters of 60 and 100 cps are included

The other outlet of the apparatus is intended for the oscilloscope and is specially adjustable for duplex oscillometry which gives special possibilities of sound segmentation The mingograph only records frequencies up to 800 cps., and that is why in duplex oscillometry the negative half wave is moved upwards by high pass filtration to obtain an intensity curve of the audio-frequency signal in respect of the highest tones. Now the positive and negative curve components are miscible to obtain the best possible segmentation curve The negative curve unit marks important fricatives and explosives, revealing the high formants hence its vast importance in phoniatric examinations.

The pitch meter is, among other things, applicable in the evaluation of the range of modulation before during and after the speech therapy Many phonastenics primarily have a small range and a fairly high-pitched voice The lessons which often train the deep chest register lower the pitch, and the modulation range is increased. Furthermore, it is possible to ascertain from the curves that the periodical duration of the single fluctuations often vary strongly before the therapy but they are almost uniform thereafter

The apparatus is devised by the experimental phonetician Børge Frøkjær Jensen, who had already made an intensity meter for the examination of human voices. The instrument is constructed with a special view to phonetic research but may also be used for the examination of volume e g. in patients with dysarthria and balbuties

In recent years, Frøkjær Jensen has worked extensively with glottography at the Phonetic Institute, Copenhagen, and he has, among other things, compared his photo-electric glottograph with the Fabre glottograph. He has prepared an article on the subject for this conference and I shall consequently refrain from detailed mention of the glottograph here.

The sound spectrograph called the Sonograph is made by the Kay Electric Company and used for analysing combined sound waves in the frequency amplitude and time components A sound signal of a maximum duration of 2.4 seconds is primarily reproduced on a magnetic disc Via a filter and a writing device the curves are drawn on calibrated paper the writer working through the range of frequency from the bottom in spiral shaped turns, during which the signal is constantly repeated. The frequency levels activated by the speech produce dark focal points and lines on the teledelto paper The apparatus offers a possibility of changes in dynamic range (sensitivity), and varying filters can also be applied according to the purpose of the examination. The basic frequency can be calculated just as the individual partial note amplitude can be established by cross section. The apparatus, the principle of which is probably of a somewhat older date, is well suited for several phoniatric purposes Examinations of pathological noise-filled voices thus show the largest distribution of energy in the lower frequency ranges, while speech therapy moves the energy concentrations upwards in the spectrum Indistinct articulation appears in broad, ill-defined formant ribbons, while a normal pronunciation manifests itself in narrower and separated inkings. In several neurological speech complaints, deviating intensities and time conditions are further more noticeable in connection with the individual sounds.

For industrial and medical purposes, Brüel & Kjær have during the past year or so made a "parallel analyser" for spectral examinations.

The prototype contains 38¹/₃ octave filters with parallel inlet in the range of 22 cps to 45 kcps. The spectrogram appears as filtration columns on a 14-inch cathode oscilloscope screen, on which the abscissa draws the frequency and the ordinate the sound volume in dB. The instrument works with sound-spectrum variations as low as 0.02 second and is thus particularly suitable for vocal examinations. It is able to work with different time constants and comprises four tunings for column adjustment (dynamic range). The apparatus can be fed from tape recorder or microphone, and the picture on the screen frozen by the storage principle. Its outlet signal is transmittable in BCD code to puncher computer or writer and the sound-volume response of the individual filters are direct readable on a digital band-level indicator. Probably the instrument can be made cheaper for our purposes, which do not require the extremely large frequency range. Furthermore, somewhat narrower filters would be of advantage for phoniatric purposes.

The Electro-aerometer records the quantity of air which, during a defined time unit, passes in and out through the mouth and nose. In addition to these four channels the apparatus has a fifth from a built-in microphone.

The apparatus has been made by Professor Svend Smith, Ph.D. and Assistant Professor Børge Frøkjær Jensen, M.A. and it is well suited for qualitative and quantitative evaluation of the rhinophonies and of the medical and pedagogic results of their treatment. The principle of this instrument is that the air flow is converted to a pressure on a rubber valve (Monyo), the opening degree of which is registered by means of a ray of light, which is collected by a photodiode through the lumen of the valve. In addition to the four flow transducers and the microphone, it contains corresponding amplifiers, through which the signal is carried to the mingograph. Besides the flow examinations, the instrument can also be used for judging the vital capacity of the lungs, etc.

Pressure measurements are also of great interest to phoniatricians in their work. Investigations in and over the oesophagus in laryngectomized patients are of importance to the prognosis in relation to oesophageal speech, and evaluation of the sub-glottic and pharyngeal pressure is of importance in other complaints. A new pressure meter made with a transducer particularly suitable for our purposes, is sold under the name of "Manophone.

In phoniatric diagnosis, stroboscopy is a necessary supplement to the indirect laryngoscopy. Several instruments with synchronous microphone control, tone-generator control and phase displacer are now on the market. The method offers a possibility of a differentiated judgement of the pattern of fluctuations, the shape of the vocal cords, the amplitudes, the edge displacement, the glottis inlet and the time relationships of the opening and closing phases, and it contributes in particular to an early diagnosis of firm vocal-cord tumours including cancer. The apparatus is a good help among other things, in the judgement of hormonal voices and the regression of recurrent paresis.

Phoniatrics is a specialty occupying an intermediate position in relation to several others, but most closely related to otorhinolaryngology. It often has to benefit from the services of neighbouring specialties, methods and techniques of examinations, but first and foremost it must seek its own tests, objective measuring methods for the evaluation of the qualities of the voice, speech and language.

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ULTRASONIC RECORDING OF THE VIBRATING VOCAL FOLDS

A PRELIMINARY REPORT

C. H Hertz, K Lindström and B Sonesson

From the Department of Anatomy University of Lund and the Department of Electrical Measurements Institute of Technology Lund, Sweden

The ultrasonic echo method has been used to study the vibratory movements of the vocal folds. A special transducer developed for this purpose was used together with commercial ultrasonic equipment designed for heart diagnosis. Well-defined curves of the movement of the vocal folds have been recorded, which confirm the results obtained by other methods. The advantages of the ultrasonic method over other techniques are:

a Continuous recording of vibrating vocal folds.
b No interference with the articulatory movements of the tongue and the mandible
c. No discomfort to the patient, and simplicity of application.

The method can be expected to improve appreciably in definition and resolution if specially designed ultrasonic equipment is used.

In the study of normal speech as well as vocal disorders, the vibratory movements of the vocal folds are of great interest. Several methods have been developed with the object of visualizing the rapid vibratory movements of the vocal folds.

In the present paper a preliminary report will be given of a laryngologic ultrasonographic method for studying the vibratory movements of the vocal folds. The advantage of this method is that a continuous recording can be made of the vibrations without interfering with the articulatory movements and without putting any disturbing instruments into the mouth or pharynx In fact, the ultrasonic technique is very suitable for studying the larynx because it contains air which gives a maximum reflection of the ultrasound beam

Method

The ultrasonic echo method has been used for the study of the vibrating vocal folds. The measurements are made with a modern version of the ultrasound reflectoscope developed for non-destructive testing of materials (Firestone, 1945) This technique uses short ultrasound pulses generated by an electrically excited ultrasound transducer and delivered to the material under investigation. This is done by pressing an ultrasonic transducer directly against the surface of the material under investigation. A good acoustical contact is secured by using a thin intermediate layer of oil or ultrasonic jelly between the transducer and the surface of the material.

Each time an acoustic pulse is transmitted, the electron beam of a cathode-ray tube encased in the reflectoscope starts moving from the left to the right side of the screen in the x-direction. At the same time, the beam is deflected in the y-direction during the emission of the sound pulse. If the material contains any boundaries which are impinged upon by the sound pulse and which reflect part of the sound back in a direction opposite to its original this reflected ultrasound pulse (echo) will reach the transducer which then acts as a microphone and converts the sound pulse into an electrical pulse. This pulse, after amplification, again deflects the electron beam in the y-direction. Since normally both the sound and the electron beam are moving at constant

speed, the distance to the reflecting boundary can be measured in this way. The method was thoroughly discussed in the paper by Hertz (1967).

Transducer

The vibratory movements of the vocal folds are rather complex, especially in low-tone frequencies. Large surfaces of the vocal folds then contact each other during the closure period of the vibratory cycle. When the opening of the glottis is to occur the complete separation of the vocal folds does not take place instantly: it starts from underneath, the opening progressing upwards, and not until the upper parts have separated does the glottis open (Smith, 1954). To be able to resolve movements from different parts of the vocal folds, a very narrow ultrasonic beam must be used.

In order to decrease the width of the ultrasonic beam at the medial surface of the vocal fold, a transducer was used formed as a focusing bowl with a diameter of 18 mm, a focal length of 24 mm, and a resonance frequency of 2 MHz (Brush Clevite BFB/ 2C24–5). The material in the transducer PZT.5A, a modified lead zirconate titanate, provides a good compromise between transmitting efficiency and receiving sensitivity for the transducer together with a relatively high mechanical damping.

Apparatus and Recording Technique

The "Ekoline 20" ultrasound reflectoscope, manufactured by the Smith Kline Instrument Company, Philadelphia, U. S. A., was used in this investigation. The pulse repetition frequency for this apparatus was 1000 Hz, and the pulse length was variable between 0.3–3 × 10 sec. The ultrasound frequency used was 2 MHz. The apparatus was equipped with some electronic facilities for signal processing, such as time-varying gain (depth compensation) to compensate for ultrasound absorption in tissue and a possibility of delayed sweep, so that

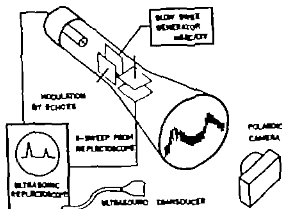


Fig. 1. Block diagram of the recording method in which the ultrasonographic recordings of the vibrating vocal folds are directly displayed on the screen of a cathode-ray tube and photographed with a Polaroid camera.

echoes along the x-axis can be studied enlarged and in detail.

Because of the rapid vibratory movements of the vocal folds, only information of limited value can be obtained by direct inspection of the reflectoscope display. Thus, the movements of the echoes have to be recorded in the same way as is done in the ultrasound-echo technique for heart diagnosis. For the recording of ultrasound cardiograms, three different techniques are in use: the photographic method, the direct recording method, and intensity modulation of cathode ray tube (Hertz, 1967). As the vibratory frequency of the vocal folds is much higher than the frequencies occurring in heart recording, the intensity modulation method has been used in this investigation. Fig. 1 shows that, in this method, the intensity of the electron beam in a cathode-ray tube is modulated by the echo signals from the reflectoscope in such a way that it appears on the screen only when an echo is present (Hertz & Edler, 1956). The sweep voltage from the ultrasound reflectoscope is used to deflect the electron beam along the negative y axis for every ultrasound pulse. Now if the time base of the cathode-ray oscilloscope is running at a suitable deflection speed, say 5 to 10 millisec./div., the movement curve of the vocal fold can

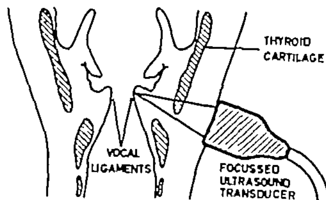


Fig. 2. Schematic picture of the application of the transducer to the neck of the patient for recording *movements of the vibrating vocal folds.*

immediately be observed on the screen To get better amplitude of the movement curves a delayed sweep can be used to enlarge the desired portion of the echo on the CRT screen. For measurement the screen can be photographed with a Polaroid camera.

In the arrangement used a Tektronix 565 double beam oscilloscope has complemented the reflectoscope for the time-motion representation of the movements of the vocal fold

The main drawback of this arrangement is the relatively low frequency of the transducer which could be higher in order to reduce the physical size of the transducer This could give a smaller ultrasound beam at the medial surface of the vocal fold. The repetition pulse frequency of 1000 Hz of the reflectoscope used gave only about 10 measurement points in each vibratory cycle, which is rather low A better repetition frequency for this purpose would be between 6 000 and 10 000 Hz, which could be obtained with modern electronic circuits.

The transducer probe was positioned at the thyroid lamina about 1 cm below and lateral to the thyroid prominence corresponding to the horizontal level of the vocal folds. The probe was placed almost perpendicular to the surface of the neck as shown in Fig. 2 The male subject, who had a normal voice without any organic or functional disturbances in his larynx was instructed to produce a sustained vowel keeping the intensity and frequency of tone constant. Different vowels were also pronounced to see if any differences in the echo pattern could be observed

RESULTS

In Fig 3 a laryngologic ultrasonogram is given showing the structures within the vibrating larynx The tone frequency of the voice was about 100 Hz and the intensity medium. At the top of the figure the echoes from the thyroid cartilage are seen, and below that, the oscillating echoes from one vocal fold. The vibratory amplitude of the vocal fold is measured to about 1 mm and in the trace the upper peak represents the open position of the vocal fold and the lower part of the trace the closed position The regular shape of the curve corresponding to the vibratory cycles is found throughout the recordings.

In the echo trace from the vocal fold, the closed interval in each cycle can be seen as a horizontal level more distinct in some cycles and less in others. The most distinct point in the trace is the top, corresponding to the maximally opened position of the vocal fold whereas the moments of opening and closing the glottis are less distinctly marked.

The opening phase of the vibratory cycle is measured to about 3 msec, the closing phase to 4 msec and the closed interval to between 2 and 3 msec. This means that the open quotient is 0 7 and the speed quotient 0 8

For different vowels, the laryngologic ultra-

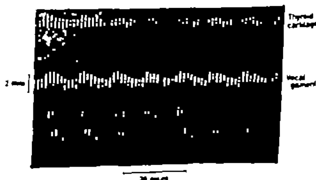


Fig. 3 Ultrasonic recording of the vibrating vocal fold obtained with the apparatus shown in Fig 2.

sonogram seemed to have the same appearance, but in the present study no systematic analysis was made on this problem. Further studies are needed for a more conclusive opinion.

DISCUSSION

In the present study the ultrasonic glottogram had the same appearance as that obtained with the photo-glottographic method (Sonesson, 1960). It means that the ultrasonic method reflects the vibratory movements of the vocal folds, and especially the parts of the vocal folds which have the greatest amplitude, i. e. the vocal ligaments.

Our ultrasonic glottograms also agree well with the calculated displacement curves, which Minifie *et al* (1967) obtained by integrating the velocity curves recorded by the Doppler frequency-shift method. The present results seem to indicate that the movement of the vocal folds can be recorded by using the ultrasonic echo method, but that the commercially available apparatus generates too low ultrasound frequencies as well as too low pulse rates to give good definition and details of the movement of the vocal folds. Because of this, it is planned to develop ultrasonic equipment specially intended for this purpose.

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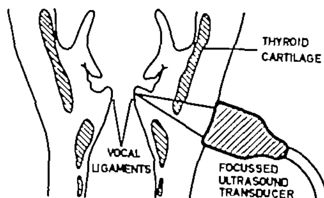


Fig. 2 Schematic picture of the application of the transducer to the neck of the patient for recording movements of the vibrating vocal folds.

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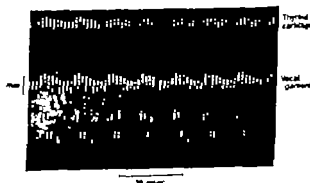


Fig. 3 Ultrasonic recording of the vibrating vocal folds obtained with the apparatus shown in Fig. 2.

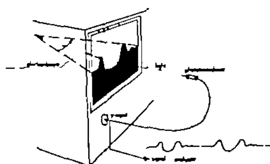


Fig. 2. Perspective view of the set-up.

in the lower and dark in the upper part, a photographic recording (negative) in the scale 1 1 is made and a masterphoto is produced. This will show a dark lower and a transparent upper part and will have the desired signal part as a transitional curve.

The masterphoto is placed on the front glass of the CRT and a photo transducer is placed in the same position to the CRT as the objective of the camera before (Fig. 2) The amplified output of the photo transducer is used as a signal for the oscilloscope Y input. As the electron beam is swept horizontally on the CRT the output from the photo transducer via the vertical (Y) deflection will force the beam to follow the signal curve.

The Y input will then be a copy of the original signal part thus repeated with the same repetition as the beam sweep

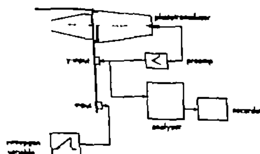


Fig. 3. Instrumentation involved: Oscilloscope photo-transducer pr -amplifier audio-frequency analyser paper recorder and external ep generator

Frequency Transformation

Using an external sweep generator (Fig. 3) with variable sweep speed and repetition, it is possible to avoid error signals due to the built in blanking of the electron beam during the fly back time and furthermore to gain a great flexibility in the choice of frequency transformation and repetition.

Reliability

In order to calculate the reliability of the method a sinusoidal signal was used. Sweep time and repetition rate were an even multiple of the period of the base frequency In the line spectrum theoretically only one of the harmonics corresponding to the base frequency should be measured, but noise limitation will give measurable values for other harmonics. In addition, unlinearities in the oscilloscope and the photo equipment will make a frequency and a phase modulation of the signal.

In this way the dynamic range was determined to be better than 35 dB, and the frequency and the phase modulations corresponding to this dynamic range were better than 15 %

Applications

Examples of the application of this metod are given below

Vowels

Fig. 4 shows 8 msec. of a Danish ae vowel cut from the exclamation "naeh" The *sweep duration* is 8 msec. producing a distance between the lines of 125 cps in the line spectrum. In the amplitude-density spectrum measurable amplitude densities in the frequency areas about 200, 500 and 1800 cps are obtained. Only the "ae -sound spectrum is present in this way and the influence due to the "n and "h" vocalization has been suppressed.

EEG

Fig. 5 shows 800 msec. (0.8 sec.) of an EEG recording. The sweep duration is 8 msec., thus producing a frequency transformation of 1 100

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A METHOD FOR FREQUENCY ANALYSIS OF SHORT TRANSIENT SOUND SIGNALS

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M Sc. E Eng.

From the Technical Department and the Department of Otolaryngology County Hospital Gentofte Denmark

A method for frequency analysis of short aperiodic signals is described and its reliability outlined. The method permits specific determination and investigation of the signal parts of interest and furthermore frequency transformation and arbitrary resolution of the frequency spectrum are obtained. Application in the speech and EEG-frequency analysis is demonstrated.

Analysing short aperiodic signals in the low frequency range includes several problems. These are

1 Frequency analysis.
2 Determination and investigation of the desired signal part.
3 Arbitrary frequency transformation of the signal to a convenient frequency range.

Frequency Analysis

Investigating short aperiodic signals, the amplitude-density spectrum of the signal is usually the primary object. Using conventional techniques, this can be measured by repeating the aperiodic signal with a known repetition frequency The periodic signal thus obtained consisting of a periodically repeated aperiodic signal is used as an input to a conventional audio-frequency analyser The analyser will then measure an amplitude-line spectrum consisting of a combination of the harmonics to the repetition frequency Using a low repetition frequency a small distance between the lines in the line spectrum will appear resulting in a good frequency resolution.

The amplitude-density spectrum of the aperiodic signal will then be the convolution of the measured line spectrum

Determination and Investigation

*Fig. 1 shows an output voltage from a micro*phone. A frequency analysis of the black part is desired. This signal part can be described and determined by its delay

The total signal is displayed on the cathode ray tube (CRT) of an oscilloscope Using a delayed sweep procedure, the desired signal part (black) can easily be fixed and presented alone on the CRT After mixing with a high-frequency carrier the CRT picture will be bright

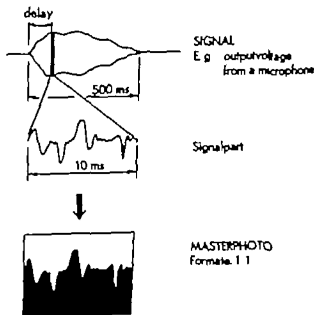


Fig. 1 Determination and investigation of the desired signal part. Production of the masterphoto.

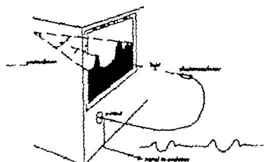


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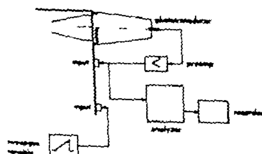


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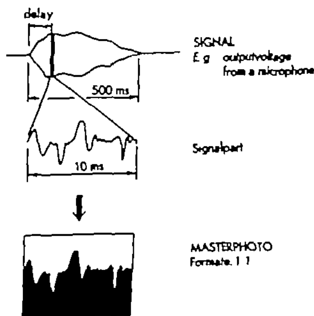


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ELECTRICAL STIMULATION OF THE HUMAN RECURRENT LARYNGEAL NERVE DURING THYROID OPERATION

K. Flisberg and T Lindholm

From the Department of Otolaryngology and the Medical Department B (Renal Clinic), University Hospital Lund Sweden

A method for identification of the human recurrent laryngeal nerv during thyroid operation is described. It is based on electrical stimulation of the nerve and recording of the muscle action potentials in the vocal muscle with needle electrode inserted through the cricothyroid membrane. The recurrent laryngeal nerve could be easily identified in all of the 13 patients (13 nerves) investigated. The motor nerve conduction velocity in the recurrent laryngeal nerve was also studied and found to be 48.6 ± 3.5 m/sec.

In his anatomical studies of the recurrent laryngeal nerve Lanz (1955) noted great variations in its course. This means that the recurrent laryngeal nerve is exposed to the risk of being damaged by incisions on the neck, especially for thyroid operations. The risk is, in particular great in re-operations, because of the excessive scars around the trachea, and also in operations for large tumours, which can displace the nerve In operations for malignant tumours of the thyroid it is often necessary to remove one or both of the thyroid lobes completely or partially It is important that the recurrent laryngeal nerve be spared in radical operation, provided that this does not interfere with the complete removal of the tumour In radical operations the nerve must therefore be identified and protected against injury Hawe & Lothian (1960) presented a series of 1011 patients, in whom the recurrent laryngeal nerve was isolated in operations for various thyroid disorders Vocal-cord paralysis developed in 28 cases and became permanent in three. According to an analysis by Meurman (1951), the risk of causing damage to the recurrent laryngeal nerve in primary thyroid surgery ranged from 0.3 % to 13.2 % in different series in re-operation the risk increased to between 10.0 % and 15.4 % The corresponding rates of complications are virtually unchanged in later reports (Wade, 1955 Riddell, 1956 Blomstedt & Rydmark, 1960 Haw & Lothian, 1960). According to Lahey (1944) and Hawe & Lothian (1960) the isolation of the nerve, in itself involves only a slight risk of injury In thyroid operations the risk of injury to the recurrent laryngeal nerve will thus be greater if the nerve is not identified and isolated.

We present here a simple and clinically usable method for the identification of the recurrent laryngeal nerve in operations. The technique applied also enabled us to study the conduction velocity in the nerve.

Previous Methods

Shedd & Burget (1966) and Shedd & Durham (1966) described an objective method of electrical identification of the recurrent laryngeal nerve. An air-inflated balloon was applied between the vocal cords and connected to a manometer On electrical stimulation of the nerve a rise in pressure in the balloon was noted, indicating muscular activity in the intrinsic laryngeal muscles. Peytz *et al.* (1965), using concentric needle electrodes, studied the muscular activity in the intrinsic laryngeal muscles through a laryngoscope or during total laryngectomy In 29 cases, the stimulation was performed through needle electrodes inserted percutaneously near the nerve, either at its cra-

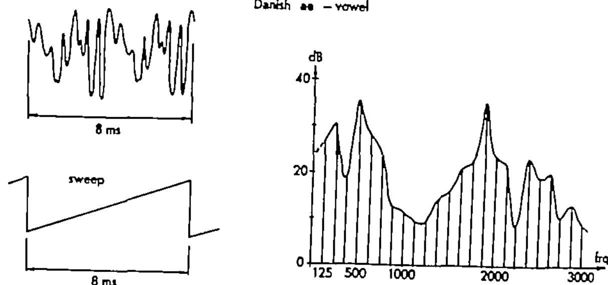


Fig 4 Analysis of a Danish ae vowel.

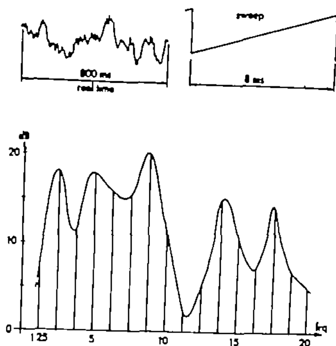


Fig. 5 EEG analysis.

and a distance beteen the lines of 125 cps in the line spectrum The EEG frequencies are transposed from the frequency range 1–20 cps into the range 100–2000 cps, permitting the use of a conventional audio-analyser Plotting the line spectrum the frequency axis is retransformed into the original range.

Most energy is obtained in the range 6–10 cps corresponding to an α-rhythm, and a smaller amount at 13–15 cps corresponding to a β-rhythm.

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ELECTRICAL STIMULATION OF THE HUMAN RECURRENT LARYNGEAL NERVE DURING THYROID OPERATION

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A method for identification of the human recurrent laryngeal nerve during thyroid operation is described. It is based on electrical stimulation of the nerve and recording of the muscle action potentials in the vocal muscle with a needle electrode inserted through the crico-thyroid membrane. The recurrent laryngeal nerve could be easily identified in all of the 13 patients (15 nerves) investigated. The motor nerve conduction velocity in the recurrent laryngeal nerve was also studied and found to be 48.6 ± 3.5 m/sec.

In his anatomical studies of the recurrent laryngeal nerve Lanz (1955) noted great variations in its course. This means that the recurrent laryngeal nerve is exposed to the risk of being damaged by incisions on the neck, especially for thyroid operations. The risk is, in particular, great in re-operations, because of the excessive scars around the trachea, and also in operations for large tumours, which can displace the nerve. In operations for malignant tumours of the thyroid it is often necessary to remove one or both of the thyroid lobes completely or partially. It is important that the recurrent laryngeal nerve be spared in radical operation, provided that this does not interfere with the complete removal of the tumour. In radical operations the nerve must therefore be identified and protected against injury. Hawe & Lothian (1960) presented a series of 1011 patients, in whom the recurrent laryngeal nerve was isolated in operations for various thyroid disorders. Vocal-cord paralysis developed in 28 cases and became permanent in three. According to an analysis by Moorman (1951), the risk of causing damage to the recurrent laryngeal nerve in primary thyroid surgery ranged from 0.3 % to 13.2 % in different series. In re-operation the risk increased to between 10.0 % and 15.4 %. The corresponding rates of complications are virtually unchanged in later reports (Wade, 1955; Riddell, 1956; Blomstedt & Rydmark, 1960; Hawe & Lothian, 1960). According to Lahey (1944) and Hawe & Lothian (1960), the isolation of the nerve, in itself, involves only a slight risk of injury. In thyroid operations the risk of injury to the recurrent laryngeal nerve will thus be greater if the nerve is not identified and isolated.

We present here a simple and clinically usable method for the identification of the recurrent laryngeal nerve in operations. The technique applied also enabled us to study the conduction velocity in the nerve.

Previous Methods

Shedd & Burget (1966) and Shedd & Durham (1966) described an objective method of electrical identification of the recurrent laryngeal nerve. An air-inflated balloon was applied between the vocal cords and connected to a manometer. On electrical stimulation of the nerve a rise in pressure in the balloon was noted, indicating muscular activity in the intrinsic laryngeal muscles. Peytz *et al.* (1965) using concentric needle electrodes, studied the muscular activity in the intrinsic laryngeal muscles through a laryngoscope or during total laryngectomy. In 29 cases, the stimulation was performed through needle electrodes inserted percutaneously near the nerve, either at its cra-

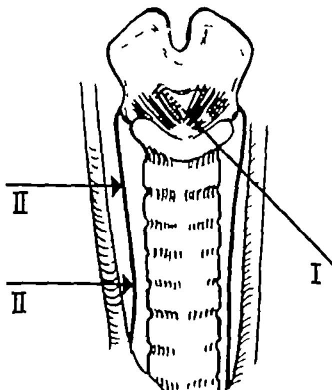


Fig. 1 Sites of the recording needle electrode (I) and the nerve stimulation electrode (II)

nially ascending branch or at the vagus nerve. After measurements on corpses, the length of the nerve in the patient was calculated, and the authors were then able also to determine the conduction velocity in the nerve in eight cases The nerve conduction velocity was 60–70 m/sec.

Electromyographic studies of the intrinsic laryngeal muscles have previously been made, for instance, by Faaborg Andersen (1957) who inserted the recording electrode into the investigated muscles through the pharynx Hiroto *et al* (1962) described a transcutaneous method for electromyographic studies of all the intrinsic laryngeal muscles. Their method was used and improved by Hirano & Ohala (1967)

Methods

We used a bipolar needle electrode, DISA type 13 K 14 (six nerves) or a bipolar electrode DISA type 13 K 33 (nine nerves) for stimulation of the recurrent laryngeal nerve The electrodes were applied direct on the nerve, cranially and caudally in the operating fiel (Fig 1) Stimuli were rectangular supramaxi mal current pulses, 0.2 msec. in duration passed from a DISA Multistim or from a DIS stimulator unit, type 14 E 11 The distanc between the stimulation sites on the nerve wa kept constant by placing a measure, 30 mm i length close to the nerve. The stimulation re sponse in the intrinsic laryngeal muscles wa recorded through concentric needle electrode DISA type 13 K 51 The needle electrode wa inserted through the cricothyroid membrane positioned so that its tip was in the vocal mus cle (Fig. 1) In most cases the position of th needle electrode could be altered so that a initially negative phase of the muscle actio potential was obtained, indicating that it wa situated in the end plate region. The muscl action potentials were amplified and recorded i a three-channel electromyograph, DISA type 1 A 69 or in a one-channel electromyograph DISA type 14 C 10 (Fig. 2) The sweep spee was 0.25 msec/mm and 0 1 msec/mm, re spectively The conduction velocity in the nerv could be determined, as the distance between th two stimulation sites and the difference betwee the conduction times from the two sites wer

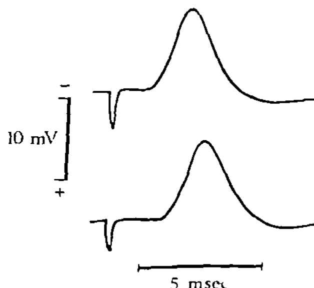


Fig. 2. Action potentials in the vocal muscle under stimulation of the recurrent laryngeal nerve at two different sites 30 mm apart.

known. The temperature at the nerve was recorded in 10 cases with an Electric Universal Thermometer type TE 3 (Ellab Copenhagen) As applicator was used an electrode with a thermo-junction (type K 8)

Material

Thirteen patients (15 nerves) were investigated during operation for thyroid tumours. The average age of the patients, 12 woman and one man, was 47 6 (26–68) years. Eight of them (eight nerves) were operated on for adenoma of the thyroid and 5 (seven nerves) for cancer of the thyroid. In four of the latter the investigation was made at re-operation. The type of anaesthesia was the same in all the cases and consisted of neuroleptic anaesthesia induced with Leptanal® plus Dridol® nitrous oxide and oxygen after premedication with atropine.

RESULTS

The recurrent laryngeal nerve was easily identified in all the cases.

Motor-nerve conduction velocity in 15 nerves averaged 48.6 ± 3.5 m/sec (S.D 13 7 m/sec) Stimulation of the nerve at the cranial site evoked a muscle action potential with a latency averaging 1 8 ± 0.07 msec. (S.D 0.26 msec) The temperature at the nerve was 34 2 ± 0.3 C

A thorough examination of the mobility of the vocal cords was made in all the cases before and after operation In none of the cases was any form of paralysis or trauma of the vocal cord observed.

DISCUSSION

Lahey (1944) Capps (1958), Elner et al. (1968) and others have all emphasized the importance of identifying the recurrent laryngeal nerve in any type of thyroid operation. Often the nerve is readily identified, but the procedure can cause the surgeon difficulties. The technique described here permits exact identification of the recurrent laryngeal nerve at dissection, and nerve injury can thus be avoided.

In two cases it was noted that the cricothyroid muscle contracted in response to stimulation of the recurrent laryngeal nerve. The contraction was strictly unilateral. This finding would probably mean that the cricothyroid muscle can be innervated also from the recurrent laryngeal nerve. However, this abnormal innervation of the cricothyroid muscle was seen and described more than a century ago by Bach (1834) after anatomical preparations: Rarissime tandem nervus recurrens ramum internum ad musculum cricothyreoideum mittit" Bach noticed this type of innervation in one of eight investigated corpses. A reflex stimulation response in the cricothyroid muscle over the superior laryngeal nerve through an afferent impulse in the recurrent laryngeal nerve is another possibility as, according to Mündnich (1956) there are sensory nerve endings in laryngeal muscles of man. An argument against this hypothesis is that contraction of the cricothyroid muscle on stimulation of the recurrent laryngeal nerve occurred in only two out of our 13 patients.

The motor-nerve conduction velocities observed were lower than those reported by Peytz et al (1965) But they used a somewhat different technique: they stimulated the nerve percutaneously and extrapolated the conduction distance from measurements on corpses. On the other hand, it may be noted that the segment over which we measured the conduction velocity was only 30 mm, which introduces a factor of uncertainty in the measurements.

We stimulated the recurrent laryngeal nerve during operations in which the nerve was dissected free and consequently exposed to some degree of chilling. The temperature of the nerve was found to be about 3 C lower than normal body temperature If the influence of temperature on conduction velocity in the recurrent laryngeal nerve were the same as in the ulnar nerve (2.4 m/sec C) (Henriksen,

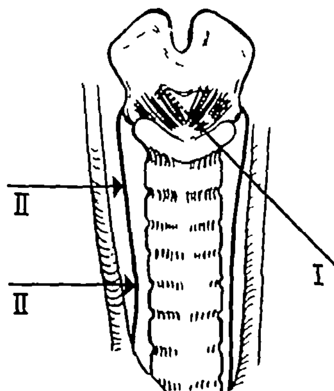


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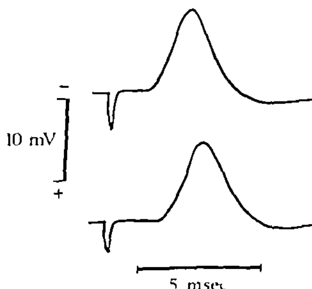


Fig. 2. Action potentials in the vocal muscle under stimulation of the recurrent laryngeal nerve at two different sites 30 mm apart.

muscle relaxant is used for the intubation in order to avoid curarization of the patient during the stimulation.

We have employed this procedure in operations for thyroid adenoma, in which injury to the recurrent nerve might be caused, and, in particular for thyroid cancer in which total thyroidectomy is performed, or total hemi-thyroidectomy on one side and partial on the other

U Sirala. The anatomical preparation of the recurrent nerve may not be necessary to avoid impaired nerve function in ordinary goitre cases. It is indicated in carcinoma—and in the difficult cases. It is important to investigate the laryngeal function pre- and postoperatively—otherwise a number of lesions will remain undiagnosed. Phoniatric treatment of the voice improves the prognosis considerably

1956) the nerve conduction velocity transposed to normal body temperature would be on an average, 56 m/sec.

As some malignant diseases can produce neuropathy (Croft & Wilkinson 1965) we compared the nerve conduction velocities in our five cases of thyroid cancer with those in the eight cases of non-malignant thyroid adenoma no difference was noted.

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DISCUSSION

H Rasmussen In the Department of Otolaryng ology of the Finsen Institute Copenhagen, we have, for nearly 2 years, used electrical stim ulation of one or both recurrent nerves i certain thyroid operations, with simultaneou recording of action potentials from one o both vocal cords. A DISA Multistim and elec tromyograph are used in the procedure.

After intubation of the patient, a concen tric or bipolar electrode is placed in one o both vocal cords by means of a Negus laryng oscope inserted in front of the tube. The elec trode is placed a little anteriorly to the middl of the vocal cord where the end plate region is During the operation we stimulate the re current nerve. Its course is followed by moving the electrode until potentials are obtained at the lowest intensity which means that the stim ulus is delivered on or around the recurrent nerve. This procedure has proved useful in avoiding lesions of the nerve A short acting

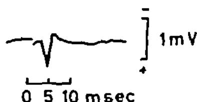


Fig. 1 Potential from the right vocal cord on stimulation of the right recurrent nerve by 11 μV amplification 100 μV sweep speed 1 msec/mm stimulus duration 0.1 sec.

in greater detail. A concert singer comes to a doctor's office. She complains that she is completely hoarse. To the doctor the voice sounds clear and beautiful, though there does appear some cracking at the pitch of e³ (659 cps.) The vocal cords seem normal. The next patient, a labourer has come to have wax removed from his ears. The patient insists that he is otherwise perfectly healthy. In the doctor's opinion, his voice sounds hoarse and in the examination, cancer of the larynx is diagnosed. It is a well-known and unfortunate fact that, for instance, cases of laryngeal cancer generally come under treatment only when the disease has reached an advanced stage. Hoarseness (as an acoustic phenomenon) is not regarded so much as a symptom of a disease but as a personal characteristic, like one's handwriting or red hair (cf. the nickname given to a person with a hoarse voice: 'Croaky') In ancient times, the voice was regarded as something "körperlich" or bodily. Besides, as a symbol of sexuality hoarseness has had its own prophets.

The way of using one's voice is the same as a way of life. There are ways of life which reveal themselves as hoarseness. Because of this, many voice disorders going under the name of "chronic laryngitis" are hopelessly difficult to cure. Patients willingly give up their tonsils, for example but not their harmful habits. Local treatment of such symptoms of "secondary laryngitis" (erythema, oedema, increased secretion of mucous, pachydermia[1] and even nodules and polyps by painting the throat and inhaling is approximately the same as trying to dry up a waterfall by drawing off the water below the fall instead of applying these measures above the fall. In cases of voice disorder this means that treatment should be turned away from local therapy to the realm of voice use and personal problems.

Personal problems show themselves in the voice in many ways. In aphonia psychogenea, the patient suddenly becomes hoarse, or starts whispering, for an emotional reason. Nevertheless, coughing is possible, which is a sign that there is no paralysis of the organ. This has been held to be a symptom of a desire to kill, to die, or to be unborn (Moses, 1954). Reality is experienced as too oppressive, and so there is an escape into regression. One manifestation of this is dysphonia plicae ventricularis (Arnold & Pinto, 1960) in which a phylogenetically older function gains the ascendency in the functioning of the larynx. The result is that the ventricular folds are compressed in phonation, so that the vocal cords cannot function. One form is dysphonia spastica, which Kiml (1963) divided into six subgroups. Features of these situations are relatively small local changes in the vocal cords, spastic, tight, snatchy breathing and voice. "Communal vocalisation" (Kallen, 1959) for instance, shouting at a football match, can at times be easily managed. On the other hand, in situations which are in one way or another significant to this person, communication by means of the voice is very difficult. These cases "very often sail under the false flag of chronic laryngitis"

Even if simple forms are the exception and complex forms the rule, from the practical point of view one should bear in mind that laryngitis caused by infection is worst in the morning and that caused by voice strain is worst in the evening. A psychogenic voice disorder changes suddenly and apparently inconsistently. A hormone-based disorder appears to remain more stable.

A function of a definite kind proceeds most economically if its structure is optimal. An exception to this "functional optimum" means that the voice disorder is becoming latent. A change in the function is influenced by psychological factors, habits, "voice culture", a change in the structure caused by infections, and also by different hormone disturbances, growth of the larynx, etc. If the function does not follow the growth of the larynx, the consequence is the disorder of the mutational voice. In boys, the voice breaks

1 The surgical removal of these is sometimes sufficient for improvement of the voice but nevertheless it is only treatment of symptom.

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PHONIATRIC VIEWPOINTS ON HOARSENESS

A Sonninen

From the Phoniatric Department Central Hospital Jyväskylä Finland

Many things can be indicated by hoarseness, in the examination of which at least four different levels, not to be confused with each other must be taken into account. (a) the psychological, (b) the acoustical, (c) the patho-physiological, (d) the patho-anatomical A description of the above levels will be followed by a discussion of the mechanism of voice strain. A new theory is formulated, according to which vocal nodules develop chiefly as a result of excessive loading on the tenser ligaments in incorrect open voice phonation.

Hoarseness is a general term for voice symptoms which may be caused by any disease or disorder of the larynx Although hoarseness is relatively common statistics concerning it are scanty and they are very defective and even controversial Whereas according to Nadoleczny (1926) as many as 41 6 of schoolchildren had chronic hoarseness, in an extensive investigation in the American Speech and Hearing Association s Committee Report on the Midcentury White House Conference on Children and Youth (1952) the figure for the 5–21 age-range was only 0.2 %

There are several reasons for the defectiveness of the statistics. In the phylogenetic sense phonation is a new secondary and thus unstable function In the pressures of social intercourse and the demands of civilisation the larynx has, to a considerable degree been forced to change from its original primary functions of swallowing and breathing In adapting itself to phonation the larynx in some respects has to work "against nature" In phonation one has to learn to free oneself from some of those disturbing reflexes which are connected with the primary functions, of which the most important is surely the mechanism of swallowing (Ruth, 1952) The most economical, the most effective and furthermore the least tiring use of the vocal cords is, for this reason, by no means inborn, but it must be learnt by everyone, frequently with difficulty and it demands practice Seeing that the prerequisites for learning the ability to use one s voice musicality anatomical conditions, illnesses, etc. vary and the prototypes which influence the use of the voice right from the earliest childhood as well as one s culture etc regulate the learning process, one should not be surprised by the variations in the human voice and in its use nor by the fact that some people do not learn to use their voice "correctly" at all Another reason for the defectiveness of the statistics is to be found in the vague and multi layered nature of the concept of hoarseness.

In this paper I want to throw some light on this question by examining four different levels of hoarseness, namely the psychological, the acoustical the physiological and the anatomical

1 On *the psychological level* the way in which the patient himself experiences everything is decisive *In contrast to people in the* worlds of bel canto and the art of public speaking, the man in the street does not usually regard hoarseness as anything peculiar Let the following two cases illustrate this question

in greater detail. A concert singer comes to a doctor's office. She complains that she is completely hoarse. To the doctor the voice sounds clear and beautiful, though there does appear some cracking at the pitch of e^4 (659 cps.) The vocal cords seem normal. The next patient, a labourer has come to have wax removed from his ears. The patient insists that he is otherwise perfectly healthy. In the doctor's opinion, his voice sounds hoarse and in the examination, cancer of the larynx is diagnosed. It is a well-known and unfortunate fact that, for instance cases of laryngeal cancer generally come under treatment only when the disease has reached an advanced stage. Hoarseness (as an acoustic phenomenon) is not regarded so much as a symptom of a disease but as a personal characteristic, like one's handwriting or red hair (cf. the nickname given to a person with a hoarse voice: 'Croaky') In ancient times, the voice was regarded as something 'körperlich' or bodily. Besides, as a symbol of sexuality hoarseness has had its own prophets.

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in greater detail. A concert singer comes to a doctor's office. She complains that she is completely hoarse. To the doctor, the voice sounds clear and beautiful, though there does appear some cracking at the pitch of e⁴ (659 cps.) The vocal cords seem normal. The next patient, a labourer, has come to have wax removed from his ears. The patient insists that he is otherwise perfectly healthy. In the doctor's opinion, his voice sounds hoarse and in the examination, cancer of the larynx is diagnosed. It is a well-known and unfortunate fact that, for instance, cases of laryngeal cancer generally come under treatment only when the disease has reached an advanced stage. Hoarseness (as an acoustic phenomenon) is not regarded so much as a symptom of a disease but as a personal characteristic, like one's handwriting or red hair (cf. the nickname given to a person with a hoarse voice: 'Croaky'). In ancient times, the voice was regarded as something körperlich or bodily. Besides, as a symbol of sexuality, hoarseness has had its own prophets.

The way of using one's voice is the same as a way of life. There are ways of life which reveal themselves as hoarseness. Because of this, many voice disorders going under the name of chronic laryngitis are hopelessly difficult to cure. Patients willingly give up their tonsils, for example, but not their harmful habits. Local treatment of such symptoms of secondary laryngitis (erythema, oedema, increased secretion of mucous, pachydermia[1] and even nodules and polyps) by painting the throat and inhaling is approximately the same as trying to dry up a waterfall by *drawing off* the water below the fall instead of applying these measures above the fall. In cases of voice disorder this means that treatment should be turned away from local therapy to the realm of voice use and personal problems.

Personal problems show themselves in the voice in many ways. In aphonia psychogenica, the patient suddenly becomes hoarse, or starts whispering, for an emotional reason. Nevertheless, coughing is possible, which is a sign that there is no paralysis of the organ. This has been held to be a symptom of a desire to kill, to die, or to be unborn (Moses, 1954). Reality is experienced as too oppressive, and so there is an escape into regression. One manifestation of this is dysphonia plicae ventricularis (Arnold & Pinto, 1960) in which a phylogenetically older function gains the ascendency in the functioning of the larynx. The result is that the ventricular folds are compressed in phonation, so that the vocal cords cannot function. One form is dysphonia spastica, which Kiml (1963) divided into six subgroups. Features of these situations are relatively small local changes in the vocal cords, spastic, tight, snatchy breathing and voice. "Communal vocalisation" (Kallen, 1959) for instance, shouting at a football match, can at times be easily managed. On the other hand, in situations which are in one way or another significant to this person, communication by means of the voice is very difficult. These cases "very often sail under the false flag of chronic laryngitis"

Even if simple forms are the exception and complex forms the rule, from the practical point of view one should bear in mind that laryngitis caused by infection is worst in the morning and that caused by voice strain is worst in the *evening*. A psychogenic voice disorder changes suddenly and apparently inconsistently. A hormone-based disorder appears to remain more stable.

A function of a definite kind proceeds "most economically" if its structure is optimal. An exception to this "functional optimum" means that the voice disorder is becoming latent. A change in the function is influenced by psychological factors, habits, "voice-culture", a change in the structure caused by infections, and also by different hormone disturbances, growth of the larynx, etc. If the function does not follow the growth of the larynx, the consequence is the disorder of the mutational voice. In boys, the voice breaks

1 The surgical removal of these is sometimes sufficient for improvement of the voice, but nevertheless it is only treatment of symptom.

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PHONIATRIC VIEWPOINTS ON HOARSENESS

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Many things can be indicated by hoarseness, in the examination of which at least four different levels, not to be confused with each other must be taken into account. (a) the psychological (b) the acousti cal, (c) the patho-physiological (d) the patho-anatom ical A description of the above levels will be fol lowed by a discussion of the mechanism of voice strain. A new theory is formulated, according to which vocal nodules develop chiefly as a result of ex cessive loading on the tenser ligaments in incorrect open voice phonation

Hoarseness is a general term for voice symptoms which may be caused by any disease or disorder of the larynx Although hoarseness is relatively common, statistics concerning it are scanty and they are very defective and even controversial Whereas according to Na doleczny (1926) as many as 41 6 of school children had chronic hoarseness, in an exten sive investigation in the American Speech and Hearing Association s Committee Report on the Midcentury White House Conference on Child ren and Youth (1952) the figure for the 5–21 age range was only 0 2 %

There are several reasons for the defective ness of the statistics In the phylogenetic sense, phonation is a new secondary and thus un stable, function In the pressures of social in tercourse and the demands of civilisation the larynx has, to a considerable degree been forced to change from its original primary func tions of swallowing and breathing. In adapting itself to phonation, the larynx in some respects has to work "against nature" In phonation, one has to learn to free oneself from some of those disturbing reflexes which are connected with the primary functions, of which the most important is surely the mechanism of swallow ing (Ruth 1952) The most economical the most effective and furthermore the least tir ing use of the vocal cords is, for this reason, by no means inborn but it must be learnt by everyone frequently with difficulty and it demands practice. Seeing that the prerequi sites for learning, the ability to use one s voice, musicality anatomical conditions, illnesses, etc vary and the prototypes which influence the use of the voice right from the earliest child hood as well as one s culture etc. regulate the learning process, one should not be sur prised by the variations in the human voice and in its use, nor by the fact that some people do not learn to use their voice "correctly at all Another reason for the defectiveness of the statistics is to be found in the vague and multi layered nature of the concept of hoarse ness.

In this paper I want to throw some light on this question by examining four different le vels of hoarseness, namely the psychological the acoustical the physiological and the ana tomical

I On *the psychological level* the way in which the patient himself experiences every thing is decisive In contrast to people in the worlds of bel canto and the art of public speak ing, the man in the street does not usually regard hoarseness as anything peculiar Let the following two cases illustrate this question

radiates to the neck, to the ears, to the root of the nose, etc.). They are more noticeable in phonation than during silence but neuralgic and other troubles are clearly noticeable.

2. On *the acoustical level*, hoarseness must be examined from the point of view of auditory experience. The parallelism between the physico-acoustical changes and the psycho-physiological occurrences of the medium is an important area of research in the problem of hoarseness. Here one has to move between two extremes, on the one hand, research into the changes of pressure in the medium is not by itself enough, because changes of pressure need not necessarily be sound. The pressure impulses have to be such that they are capable of creating a psychic sound experience via the sensory organs. On the other hand, an experience without the equivalent vibrations of the medium is by no means sound, but an auditory illusion, a hallucination. When examining an auditory experience, it is therefore always necessary to take into account both the physical stimulant and the hearer and also the fact that the learning process as well as the psychological factor influence the creation of an auditory experience. Thus, auditory habits and the process of *learning* to hear are factors that must not be *overlooked*, even when discussing the problem of hoarseness. For example, it is a well-known fact that, far too often, patients suffering *from* cancer of the throat unfortunately come under treatment too late, partly because they have not learnt to listen for and correctly interpret the first symptom of cancer—namely hoarseness. Traditional misconceptions exist about the physico-acoustical phenomenon. More often than not one reads in papers and textbooks that frequency intensity and time *are* the physical components or parameters of speech sounds, as if the Fourier components were physical realities indeed" As a matter of fact, "the only physical reality of speech sound is the time function depicting the barometric pressure as a function of time Physical realities are the zero crossings" and " the whole pattern of nervous activity in the acoustic nerve is governed by the ability of the nerve endings to indicate zero crossings (Mol, 1962) Consequently it is extremely important to observe that the voice with its various features is in the end always a subjective experience. Objective methods can never replace or bypass subjective voice analysis. An accurate objective description of all the various vocal nuances seems to be an impossible task, at least at the moment. Just imagine attempting to describe objectively the following adjectives, for instance, all of which are used in describing the singing voice: (visual) bright, clear limpid, pale, cloudy muddy dark, (caloric sense) sultry warm, cold, icy (kinesthetic sense) strained, forced, breathy firm, tight, hushed, lilting, relaxed, scooping, sliding, wobbly biting, strident, supported, tense vibrant, resonant (anatomical) back, front, head- mouth- throat chest- nasal, naked, strangled, (instrumental) flute-like, piping; (material) metallic, brassy wooden, woolly gravelly airy (spatial) broad, narrow flat, rounded (aesthetic) beautiful, ugly pleasing, unpleasant; (taste) sweet, sugary dulcet, mellow and also the adjectives rich and luminant Vocal training and professional singing are almost entirely based on such subjective concepts. Subjective analysis is also important *in the investigation* of hoarseness. Isshiki and his colleagues (1969) observed that the ear is so far probably the most important instrument for measuring hoarseness. Using Osgood's semantic differential method, he finally selected four factors from among the 260 adjectives which describe the voice, for which he used the names Degree (D), Breathy (B), Rough (R), and Asthenic (A) which may be recognised by ear in a statistically significant way when using a 4-point scale. He recommends this method for use in clinical work. *The R*-factor is due to the cycle-to-cycle fluctuation of the fundamental frequency and appears on a statistically significant level, for instance, in cases of polyps of the vocal cords. *In* cases of cancer of the vocal cords the

in a more noticeable way than in girls, as well as more slowly and later Cracking of the voice appears relatively seldom. If a disturbance occurs in the boy s father identification, a 'permanent falsetto" may be a "tönender Beweis" (vocal evidence) of this (Moses, 1954) The same happens in a milder form in incomplete or delayed breaking of the voice It is a question of a purely functional disorder The patient plays the cello as though it was still the violin" Very often this kind of 16–18 year-old youth is taken to the doctor by his mother By pressing lightly on the thyroid cartilage in the direction of the dorsal during phonation a strong and deep man s voice is usually found immediately It is a professional error to forbid such a patient to use his voice, to send him to hospital for weeks and to say that he has "catarrh" or a "weak throat" These cases are often wrongly treated with antibiotics, as inflamed and swollen vocal cords are an integral part of this illness. In girls, the disorder of a breaking voice is evident in too low a speaking voice. This is also incorrectly diagnosed as "catarrh or "hysteria" In school, they sing in chorus second voice against" the great number of singers who sing first voice. During the time when the voice breaks, school singing might in other respects be harmful to the voice. These purely functional voice disorders are relatively common They are to be distinguished from the less common voice disorders which are caused by hormones.

A person who lives by his voice or for his voice more than other people experiences even a small change in the voice caused by external agents as a vague, frightening threat. This is the case, for example, with endogenous and iatrogenic virilizing symptoms Bauer (1968) in histological investigations, observed that the amount of muscular tissue increases in such cases, and the result is an increase in the vibratory mass. The doctor s assurances that everything is in order do not bring comfort. The result is a secondary neurotization Unfortunately the use of anabolistic steroids appears to be increasing The consequences are reflected in an increase in cases of voice disorders ("laryngitis chronica") in surgery and in the literature (Arndt, 1960 Timonen *et al* 1962, Bauer 1963 Damsté 1964) The worst thing is that voice symptoms come stealthily and much sooner than other virilizing symptoms. The deviation from the functional optimum has to be compensated for and the voice disorder remains latent until some temporary agent (a "cold" infection, voice strain, etc.) makes the symptoms noticeable. The causal connection remains unnoticed and the treatment is symptomatic. Unfortunately this kind of organic change in the voice frequently persists. Here, too prevention is more fruitful than treatment. In the opinion of Berendes (1968), it is advisable to make the patient aware of the possibility of virilizing side effects before treatment begins.

It is often likely that the doctor adopts the same attitude towards hoarseness as the patient. The patient complains of hoarseness to the phoniatrician or laryngologist, but of a completely different trouble to the doctor who gives anabolistic steroids. It is always the patient who poses the questions it is he who asks for help It is the doctor s duty to try to help him. And of course, nothing bad can be said about this. It is only important that this should be borne in mind when dealing with the problem of hoarseness.

Patients experience hoarseness in various individual ways. The reason for going to see a doctor is not always primarily an acoustic change in the voice but rather what the patient feels in his throat during phonation. Certain emotional disturbances and an uneconomical use of the voice become projected into the laryngeal area and they are experienced as "hoarseness" ("The voice becomes tired" when they mean that the larynx becomes tired.) In a carefully taken medical history it often becomes apparent that hoarseness is the same as in various paraesthesiae of the throat region (itching irritation in the throat, the need to swallow a sensation of dryness, roughness, burning, a lump in the throat, pain that

According to Nessel (1960), the most typical feature of a hoarse voice is noise above 5000 cps. Yanagihara (1964) taking into account, on the one hand, the progressive disappearance of the harmonics and, on the other the corresponding increase of the noise component, especially in the second and third formant ranges of vowels, discerned on sonograms four degrees of hoarseness.

The primary factor in auditory experience, and thus also in hoarseness, has been held to be the behaviour of the pressure impulse of the medium. If the frequency of the impulse, which determines the pitch of the fundamental frequency changes aperiodically from impulse to impulse (cycle-to-cycle) hoarseness is experienced, called in English jitter 'harshness' or 'roughness' Wendahl (1963) observed that even such a small variation as ±1 cps caused hoarseness to be experienced at a pitch of 100 cps. The hoarseness was greater if the variation was increased to ±10 cps. It was interesting that a ±10 cps variation caused a smaller sensation of hoarseness at a pitch of 200 cps than the same variation (±10 cps) at a pitch of 100 cps. This means that the same aperiodic vibration of the vocal cords sounds hoarser in a man's voice than in a woman's. Coleman & Wendahl (1967) observed that the duration of the voice signal also affects hoarseness. One semitone jitter conditions of 0.32 sec., 0.64 sec., and 0.80 sec. durations should correspond in roughness to three-semitone stimuli with approximate durational values of 0.13, 0.40, and 0.50 sec., respectively. A sound heard for a shorter time thus sounds clearer than a sound heard for a longer time, although the latter may in fact be more aperiodic than the former. Thus, we have the paradox: a rough voice is clearer than a clearer voice.

The sensation of hoarseness may be caused by cycle-to-cycle amplitude variations of the impulse without jitter. Wendahl (1966) uses the name 'shimmer' for this kind of roughness. It was noticed then that larger variations lead to greater hoarseness being experienced. It is practically impossible to differentiate between hoarseness caused by shimmer and hoarseness caused by jitter. A third factor causing hoarseness, partly containing both the foregoing factors (jitter and shimmer) are the variations in the form of the impulse, which were visible in Sonesson's glottograph (1962). In hyperkinesis, the impulse changes were more abrupt than normal, in phonasthenia the closed phase was sometimes absent, and the third type showed cycle-to-cycle variations in the relative duration (opening quotient) of the closed phase.

Of the foregoing forms of hoarseness 'vocal fry' (Michel & Hollien, 1968) is the one which is clearly distinguishable by ear. It may appear both in pathological cases and in healthy persons below the normal chest register (average vocal pitch 36.4 cps). Here the fundamental frequency is periodic and regular. The characteristic is an almost complete (over 30 dB) damping occurring between each impulse (Wendahl, 1963, 1966; Coleman, 1963). The noise peculiar to hoarseness may originate either in the glottis or elsewhere. Aerodynamic and neuromuscular phenomena occurring in the glottis are, therefore, central to the problem of hoarseness.

Cooper (1964), too, observed that in addition to random modulation, regular sinusoidal modulation can result in a sensation of hoarseness. "When the pulse train is completely regular the voice is, of course, completely monotone. If the frequency of the pulse train is varied up and down a little bit once or twice a second, this serves to break the monotone completely and produces something that is fairly close to satisfactory speech except that it tends to be sing-songy and, occasionally, the pitch goes up at the end of a sentence when it should have gone down. If the pulse train is modulated at a somewhat higher rate, on the order of 3 to 5 cycles per second, the voice is like that of an old man talking with a voice that creaks and breaks. This corresponds to what Dunker & Schlosshauer (1964) observed in a high-speed film in which the vocal cords of an old, hoarse sounding man vibrated completely symmetrically and periodically. Further

infiltrating growth has fixed the loose mucous membrane to the underlying structure. This results in the suction caused by the Bernoulli effect becoming difficult, the voice becoming breathy and the B-factor becoming more noticeable The practical result of this is, for instance that if hoarseness has continued for more than 3 weeks in a 40-year-old patient it might be a case of cancer of the vocal cords especially if there is breathiness (factor B) in the voice.

The voice is made up of a fundamental frequency and harmonics, and in fulfilling aesthetic requirements, the voice has to be governed by a certain conformity and a lack of noise element between them According to Winckel (1952, 1953) there are in a good singing voice a certain number of harmonics whose peaks must be under 1200 cps. Another smaller peak is required in the region of 3000 cps and between these two regions (1200 cps and 3000 cps) there is a trough. The harmonics are regulated apart from the resonance cavities, in a remarkable way by the frequency duration and the form of the primary impulse itself In a low pitched voice there are more harmonics than in a high pitched one, and they increase with the duration of the impulse. Changing from an open way of singing to a covered way the harmonics decrease (Winckel 1952 van den Berg & Vennard 1959 Gemelli *et al* 1954 Large, 1968 1969 Sonninen 1962 1969) which signifies a prolongation of the opening phase of the vocal cords and an increase in the consumption of air (Luchsinger 1951) Van den Berg & Vennard (1959) observed that the "ring" of the singing voice signifies a peak in the region of 2800–3200 cps, the "twang one in the region of 3000–3500 cps, whereas in a "honk" the harmonics have disappeared above 1000 cps.

Objective electro-acoustical investigations are irreplaceable for making a subjective analysis more accurate and complete

According to Berger (1937) aperiodicity of the fundamental frequency and the appearance of unharmonic (unharmonische) harmonics were peculiarities of pharyngeal-voice and recurrent paralysis. In addition the occasional splitting of the fundamental pitch into two voices or jumps between certain intervals (2:3 or 3 4) known as diplophonia, appeared Curry (1953) observed that in the voice of a post encephalitis patient the aperiodic vibrations were 37 5 % of the phonation, whereas he estimated that in a normal speaker they are only 2 7 % It was found in addition, that there was exceptional intonation in the pitch of the speaking voice and the fundamental frequency was too low According to Lafon & Cornut (1959) three kinds of bitonal sound exist. harmonious diplophonia (les sons bitonaux harmoniques) true diplophonia (les sons bitonaux vrais) and successive diplophonia (les sons bitonaux successifs) In harmonious diplophonia, the lower fundamental frequency is the subharmonic harmonic of the higher fundamental frequency This occurs in a badly controlled voice In true diplophonia, two fundamental frequencies with their own harmonics are heard simultaneously This occurs, for instance, in hypotony of the vocal cords, as the mass and tension of the vocal cords are asymmetrical In successive diplophonia, the fundamental frequency varies by a certain interval This occurs, for instance, in mutation disorders. Schönhärl (1962) came across cases of voice disorder in which both the fundamental frequency and the harmonics were missing, and there was only noise in their place This was the case, for example in functional aphonia, tumours, and different substitute voices (Ersatzstimme) In addition to the fundamental frequency only one or two harmonics and their replacement by noise may occur in cases of acute laryngitis the formation of cicatrices, papilloma, keratosis, and hyperkinesis A stronger fundamental frequency and distortion of the harmonics and their replacement by noise may occur in vocal nodules, polyps papillomata, and in cases of recurrent paresis and functional hyperkinesis. In addition, he observed bitonality in the same way as Lafon did

where, as in Rubin & Hirt's (1960) high-speed film, three mechanisms may appear: "open chink" where the rima does not close; "closed chink" where the rima closes, and "damping" where part of the rima is closed all the time and part is open. The middle register is more or less the transitional region between one mechanism and another.

Regularity of glottal air-pressure impulses and of vocal cord vibrations is a prerequisite for a clear voice. The duration of the vibration period determines the pitch of the fundamental frequency and of the harmonics and also to a large extent the number of the harmonics. The relation of the duration of the impulses to the duration of the period is called the "opening quotient" (OQ). It is "fraction of cycle during which the glottis is open/duration of entire cycle". It determines in a fundamental way the form of the voice pattern. The amplitude of the impulse determines the volume of the voice, and it also affects the number of the harmonics. In addition, the quality of the voice is affected by: (1) the speed at which the impulse reaches its maximum point. This corresponds approximately to the speed at which the glottis opens (opening phase). (2) The speed at which the impulse regains a state of inaction. This corresponds to the closing speed of the glottis (closing phase). (3) The time during which the glottis remains closed (closed phase). The term 'speed quotient' (CQ) is used for the relation between the opening and the closing phases. OQ increases with the pitch of the voice; SQ increases with the volume of the voice.

The earliest direct observations of the pathological vibrations of the vocal cords were made with the aid of a stroboscope. Thus, Maljutin observed in 1931 asymmetrical vibrations in voice disorders. A diseased vocal cord seemed to vibrate less, at times also more extensively than a healthy one. Maljutin conjectured that the reason for this was the failure of a kind of proprioceptive reflex system ("Automatismus der Stimmbänderselbstregulierung"). Maljutin did not see the vocal cords vibrating above 1000 cps. When the vibrations were missing below this level, the quality of the voice was not the same as when the vocal cords did vibrate. The dispute which dates from this time as to whether the non-vibration of the vocal cords which has occasionally been noticed is either real or only apparent seems to have been settled in favour of the latter alternative with the help of recent high-speed films (4000–8000 frames per second).

Von Leden *et al.* (1960) observed that in all benign disorders of the vocal cords (including paralysis) the vocal cords always vibrate, and that the diseased vocal cord affects the manner in which the healthy one vibrates. Tumours and oedema cause a quicker than usual damping of the vibration, whereas a slack, paralysed vocal cord vibrates more extensively than a tense, healthy one. Increased subglottic pressure adds to this difference. Differences generally appeared, exceeding the medial line in phase and amplitude but not in frequency in the vibrations between the healthy and the diseased parts. Frequent and rapid changes in the regularity of the vibratory pattern were the commonest symptom.

It has been possible to observe that the hoarser the voice, the more irregular are the vibrations, OQ and SQ of the vocal cords, cycle-to-cycle. Thus, Moore & Thompson noticed in 1965 that the random fundamental frequency shift of a hoarse person fluctuates, on an average, 7.04 cps and of a person hoarser than him, 8.69 cps.

On the basis of their research, Dunker & Schlosshauer (1964) arrived at "a scale of voice disorders in the presence of vocal cords microscopically unaltered. At the smallest injury only the course of the single vibration was disturbed (for example, a change of the glottis closure time), while the periodicity was preserved. Possibly this was a reflex influence on the muscle from the receptors of the altered mucous membrane. The next degree was demonstrated with the slight constitutional phonasthenia. Also in this case was the periodicity of vibration preserved, but checking all vibra-

more in Cooper's experiment, "at a little higher rate of modulation about 7 cycles per second, the effect is more nearly that of a vibration, and not unpleasant At higher rates *of say 15–30 cycles per second, the* speech is extremely rough and unpleasant this effect gradually fades out but is still quite noticeable even when the rate of modulating the pulse train approaches the voice pitch itself"

3 On *the physiological level* the glottis is the main object of investigation From the point of view of lung physiology the key point must be held to be the pulmonary alveolus where blood circulation and ventilation both meet. *The larynx is only one* part of the ventilating system The "key point" of voice physiology on the other hand is the rima glottidis in which the subglottic pressure the speed of the flow of air and the vibrating properties of the vocal cords (mass, tension) must be in the right relationship to each other (pneumophonic co-ordination) from the important initial moment (attack) of phonation The bulbar breathing centre appears to have the possibility of influencing this position in two ways firstly through the breathing muscles direct, and secondly through innervation to the vocal cords themselves (Kirikae *et al* 1962) Thus, the aerodynamic and neuromuscular processes are under the control of the bulbar centres The complicated aerodynamic neuromuscular processes in the glottis form a basis for the quality of the sound that is developed Isshiki & von Leden (1964) noticed that the consumption of air in a hoarse voice need not always be greater than normal The reason for this was the hyperfunctioning of the vocal cords and greater glottal resistance than usual, which is influenced in a decisive way by the outer tension of the vocal cords. The volume of the voice is increased by glottal resistance and/or increasing subglottic pressure "Changes in the muscle activity pattern directly affect the aerodynamic patterns and the final acoustic properties – the voice signal"

From the physical point of view "the principal source of energy in voice sounds comes from the self-excited oscillations of the vocal folds, caused by the flow of air between them. The primary feedback mechanism that makes possible and sustains oscillation is the Bernoulli effect" In addition, "quite important are secondary feedback paths that start with stimuli from the ear and from kinesthetic receptors in the vocal muscles. The mechanical interaction between the air flow and fold vibration is rather small, and acoustical effects become important only when strong resonances exist. In physical terms, the vocal folds may be idealized as a string of fairly constant mass, but of variable tension and length that is fastened *to its surrounding structures by tissue that adds* variable mass, stiffness, and damping" — If we consider the ligaments and muscles in the vocal folds to be similar in passive action to that of a rubber band, then it is easy to demonstrate that when such a system is stretched, the length is roughly proportional to the stretching force or tension. Thus, the frequency of vibration is changed but slightly when such a vibrator is stretched However if we deal with a much less extensible system, such as an ordinary piece of string, then the frequency of vibration depends markedly on the tension. The actual behaviour of the vocal folds appears to be a mixture of rubber-band like and *string-like in their action at higher frequencies,* whereas at lower frequencies they are more rubber band-like" (Salmon, 1964)

How then, does the vibration of the vocal cords in a *hoarse voice differ from the normal?*

The opinions of research workers as to how the vocal cords vibrate within the normal registers and in different pathological situations have lately supported each other in rather many respects. In the chest register the vocal cords are relatively slack vibrate throughout their breadth, length and depth, and the lower margin of the vocal cords is in the opposite stage of vibration *to that of the upper margin.* The rima becomes closed In a head voice the vocal cords are tense, taut and only small vibrations can be noticed in their medial margins

comes before them, however. Some unfortunate cases of carelessness still occur in this respect. Taking a sample is still the only way in unclear cases. On the other hand, taking samples unnecessarily and carelessly must be avoided as unevenness as well as a defect of the margin of the vocal cords may lead to chronic hoarseness. Cauterization should also be avoided. If a sample is not taken immediately the case must be kept under careful observation. The cytological test and an examination with a stroboscope may be helpful in determining the moment when a sample should be taken. I myself have come across three cases of hoarseness in which it was not possible to notice anything out of the ordinary with an ordinary examining mirror but in which stroboscopic examination revealed that one vocal cord vibrated noticeably less, the sample taken on the basis of this showed that it was a case of cancer. I will not on this occasion go into the various causes of hoarseness and the pathoanatomical changes connected with them, as they do not belong to the present subject. I believe that more causes of hoarseness can be found than the 50 mentioned by Jackson in 1939. Generally speaking, hoarseness is a symptom which directs the therapeutic attention of the doctor to the basic disease itself, which may be a tumour, paralysis, etc. Hoarseness alone is for him of no great importance. If the vocal cords are inflamed or swollen, it is normally regarded as a symptom of an infection, and the patient is prescribed an antibiotic cure, even a lengthy one, regardless of the fact that an antibiotic cure seldom affects the bacterial flora of the pharynx and larynx. Neither the histological, nor the clinical pattern of laryngitis is in reality purely infective. Textbook descriptions correspond more or less precisely with each other although the heading might be for instance chronic laryngitis (Thompson & Negus, 1948), "laryngopathie fonctionelle" (Tarneaud, 1950), or Phonasthenie (Flatau-Imhofer 1913 Blegvad, 1955.). Apart from laryngitis caused by a specific infection (lues, TB), it is normally a question of a tangle of multi-dimensional symptoms and aetiological factors, whatever name it may be given.

In this connection I would like to discuss one cause of voice disorders which is normally brushed aside in a couple of words, namely voice strain.

What is the mechanism of voice strain? It is most commonly held that the vocal cords striking together (coup de glotte) at the beginning of a sound and the friction between them in an incorrect use of the voice are the most important mechanisms. The significance of the vibration junctions (Schwingungsknotenpunkten) is hardly regarded any longer as being important. Tarneaud (1935) thought that the cause of vocal-cord nodules was general hypotony of the larynx musculature. The consequence of this is that the junctions of the anterior and middle thirds of the cords, where the vibration amplitude is the greatest, are in a position to strike against each other ("les deux cordes vocales vont se presser l'une contre l'autre et se choquer à chaque vibration avec le maximum d'intensité") Paludetti & Stirpe (1964), basing their view on histological investigations, wanted, in addition, to put forward the theory that the nodule would be of traumatic origin from the wrenching of vocal muscular fibrils at the level of their insertion in the inferior thyroid-arytenoid ligament. Kühn's thoughts (1959) also turn in the direction of the subepithelium. Taking histological investigations as the basis, he presents two mechanisms for injury of the vocal cords. (1) Primary injury of the mucous membrane caused by external irritants, such as tobacco smoke, dust, etc. They lead to papilloma, pachydermia, leukoplakia, and Bowen's disease under the effect of certain additional factors. (2) Primary injury of the subepithelial tissue. This is, above all, due to the incorrect use of the voice and voice strain. The result is a vocal nodule or polyp. It is remarkable that the epithelium in vocal-cord nodules, for instance, is normal, and the histological changes are seen in the subepithelial tissue

tions of a tone revealed jump-like shifts of the opening and closure time possible as an expression of a positioning weakness of the vocal muscles The cases coming next in severity also revealed definite phase differences with preserved periodicity This may be due mainly to muscular weakness. Finally in strong hoarseness there were distinct disturbances of the periodicity with large amplitude differences and continously changing glottis widths."— In these cases as further reaching disturbances of the reflex function circles must be present, with the surprising fact that instillation of a vasoconstricting compound in menthol oil temporarily resulted in a certain symmetry of the vocal-cord vibrations with normal periodicity"

What, then causes the irregularity of the vibrations of the vocal cords?

In paralysis, tumours and other organic voice disorders the mechanism appears to be easier to understand In functional voice disorders, on the other hand, organic prerequisites for regular vibrations should exist.

Dunker & Schlosshauer (1964) observed in *experiments with animals that after changing the tension of the cricothyroid muscle* momentary irregularities appeared in the vibrations of the vocal cords. Rubin & Hirt (1960) photographed with high speed films the break up of regular vibratory movement into complete chaos when an untrained singer changed from chest register to falsetto (break) In such vibratory chaos, the proprioceptive reflex system probably fails. Changes in the tonus of the muscular fibres occur which reverberate as changes in the vibratory properties of the vocal cords from one moment to the next. Voice training showed itself capable of curing this disorder Brewer *et al* (1960) *indicated in EMG* investigations a more persistent co-ordination and tonus disorder of the laryngeal muscles in cases of voice disorder These were corrected as a result of successful voice therapy It is interesting to remark that co-ordinatory disorders and hoarseness of the voice can be observed in physiological states in different phonation mechanisms of very small children (Sedláčková, 1967 Wasz Höckert et al. 1968 Lind 1965)

The observations explained above clearly seem to indicate that vibrations of the vocal cords are regulated by an inner reflex system whose temporary or more permanent failure *causes irregularities in the vibrations of the* vocal cords. According to Wyke (1969) there are three inner reflexes (1) the subglottic mucosal mechanoreceptor reflex which reacts quickly and sensitively to changes in subglottic pressure and thereby regulates the tonus of the intrinsic adductor musles (2) the laryngeal articular mechanoreceptor reflexes, of which especially the crico-arytenoid and the cricothyroid *innervated from the capsules of the* joints, are the most important These react very sensitively and quickly to the movements of the cartilages controlling the nucleus ambiguus through the tonus of the intrinsic laryngeal muscles attached to the laryngeal cartilages and (3) the laryngeal myotatic reflex system which is a slow reflex controlling the tonus of the muscles.

According to Wyke, in principle, a functional voice disorder can thus be caused by two types of co-ordinatory disorders, of which one is cortical voluntary and connected with learning and the other is subcortical, involuntary and dependent on the neuromuscular maturity of the reflex system Even if according to present-day ideas, Husson s neurochronaxia theory presented in 1950 has been unquestionably proved faulty it seems that neurological factors in a different form play a considerable part in the onset and treatment of voice disorders In future investigations of voice disorders one ought to delve even more thoroughly *into such neuro-phoniatric problems.*

4 On *the patho-anatomical level* the histological and cytological examination of the vocal cords occupies a central position in the problem of hoarseness. *But the examination* of the larynx with the help of a mirror which every doctor must be able to perform,

the ligaments prevent further stretching of the vocal cords (Sonninen, 1954 1956, 1962, 1969 van den Berg, 1960 Arnold, 1961 Rubin & Hirt, 1960 Damsté, 1968). From the moment when the voice rises, another mechanism has to be brought into action (cf. head-voice mechanism) We know from experiments that a high voice is more tiring than a low voice, and that at a high pitch the voice easily becomes a shout. If we wish to conserve the voice, it is advisable to speak with a low voice, when the vocal cords are less taut, and it is easier to speak softly In raising the pitch in singing, one has to learn to cover" the voice above a certain pitch. The "open way of singing, which comes naturally tires the voice. When the voice rises in the open way of singing, the larynx rises and tautens. Subglottic pressure is increased, and the result is that the higher the singing pitch the more the voice shouts. Then, at a certain point, the voice breaks and becomes completely different, thin and "falsetto-like

In the covered manner of singing, the larynx does not rise as the voice rises, but remains near the inactive level. I have been able to confirm in my x ray measurements that in phonation the vocal cords are shorter and thinner the sinus Morgagni is larger and the larynx is nearer the resting level than when singing at the same pitch in open singing. In open singing, the vocal cords are longer and thicker the sinus Morgagni is smaller and the larynx is more raised. Thus both the external and the internal larynx muscles are more contracted in open singing than at the corresponding pitch in covered singing. In covered singing, there are fewer harmonics than in the corresponding open singing (Winckel, 1952 van den Berg *et al* 1959 Gemelli *et al* 1954 Sonninen, 1962, 1969 Large, 1969) i.e. the OQ must be smaller in open singing than in covered singing. Luchsinger observed that the air consumption is smaller in open singing than in covered singing. Taking into account also Ishiki s and von Leden s observations, it seems evident that in an open manner of delivery in which the larynx muscles are greatly contracted and the air consumption is small, glottal resistance is greater than in the covered manner of delivery

The above observations seem to support my hypothesis in every way The open-voice mechanism resembles my example Case B and the covered-voice mechanism Case A. In the more primitive open-voice mechanism, voice strain is directed above all to the vocal ligament. When the injury to the ligament is great enough, the consequence is a secondary injury of the subepithelial tissue. Histological research has shown that in a vocal-cord nodule the epithelium is normal, and the changes occur in the subepithelial tissue. This appears to add further support to my hypothesis. It would be interesting to know if the primary changes in an incipient vocal-nodule case are to be found in the vocal ligament.

According to my hypothesis, the mechanism of an incorrect use of the voice injures the supporting tissue first. As it is known that collagen degeneration caused by mechanical trauma appears in degeneration of the inter vertebral disc in the peripheral layer of fibrils, as a consequence of which there are reactive infectious changes in the surrounding tissue the thought occurs whether in vocal-cord nodules, too the primary cause could be collagen degeneration, a kind of "lumbago laryngis" Much additional research is, of course, needed before this kind of tentative hypothesis can be proved right or wrong.

In the foregoing I have dealt, principally as a phoniatrician, with some problems which are, to my mind, essentially connected with hoarseness. I would, finally like to stress once again that hoarseness in itself is no simple concept, but that the problems connected with it should be dealt with on at least the four levels I have presented here.

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What, then is the mechanism of the kind of voice strain which first injures the subepithelial tissue? Friction hardly comes into the question.

At the conference organised by the New York Academy of Sciences in 1966 the subject under discussion was. "The external frame function in the control of pitch in the human voice" On the basis of my investigations, I formulated a hypothesis according to which "vocal nodules develop chiefly as a result of excessive loading on the tenser ligaments in incorrect open-voice singing" According to this theory the most important element is the injury of the vocal ligament itself not the injury of the subepithelial tissue or of the muscular fibrils I would now like to present this theory of mine in somewhat greater detail

From high-speed films we know that the upper margin of the vocal cords and the vocal ligament rotate and that the rotating vibration amplitude is greatest at the junction of the anterior and middle thirds of the cord. As the voice rises the vocal ligament is tautened and the movement becomes smaller and faster At the same time the vocal ligament lengthens.

Case A Let us imagine a vocal ligament which has a certain tension, and mass, as a piece of string of a certain length When the wind moves this piece of string its speed of vibration is F_1 (Fig. 1)

Case B The piece of string is tautened, so that the tension increases. Its length becomes greater the vibration amplitude decreases, and the vibration frequency increases ($F_2 > F_1$) If a suitable amount of additional mass is added to this tautened piece of string the vibration frequency reverts again to the Case A frequency ($F_2 = F_1$) but the tension the length, and the mass in Case B are still greater than in Case A. My hypothesis is as follows the tautened and loaded piece of string will break sooner than the string in Case A, although both have the same vibration frequency

We know that the vocal-cord muscles have anatomical possibilities of increasing the mass of the vocal ligaments when contracted. This

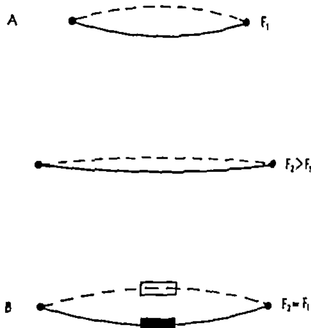


Fig 1 Two possible habits of vocal ligament vibrations: Case A correct and Case B "incorrect" The tautened and loaded vocal ligament (Case B) will "break sooner (resulting in vocal nodules) than the vocal ligament in Case A, although both have the same vibration frequency

presumably explains the irregularities of the vocal-cord vibrations that appear in tonus disorders of the muscle It is not really of great importance whether the muscular fibrils are directly attached to the vocal ligament or not. The most important thing is that connective tissue fibrils from the vocal ligaments protrude between the fibrils of the thyroid-arytenoid muscles, which makes it possible for the muscular tissue as it contracts, to engage its own mass in the vibratory movements of the vocal ligament to the same extent as the muscular fibrils contract. Let us think of the vocal ligament as a boat rocked by the sea. Someone on the jetty need not hold on to the boat with his hand If there is a string leading from the man standing on the jetty to the boat and the string is loose the boat rocks freely If the string is tautened, the boat begins to pull with a rocking rhythm at the person who is tautening the string, and at the same time the movement of the boat itself subsides.

The vocal cords are slack and short when the voice is low They tauten and lengthen as the voice rises right up to the moment when

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JUDGING THE MOVEMENTS OF VOCAL CORDS IN LARYNX PARALYSIS

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In paresis of the recurrent laryngeal nerve the homolateral vocal cord cannot adduct or abduct, but some of the phonatory movements can still be seen in stroboscopic light or on the high-speed film A discussion of the conclusion which can and also of those which cannot be drawn from the return of the missing phonatory movement of the paretic vocal cord the glottic wave is presented.

The larynx has a number of different functions of which the respiratory and the phonatory ones are the most important. It is essential for respiration that the vocal cords can be abducted in order to be out of the way for the air stream and that they can be adducted in coughing For phonation the vocal cords have to be adducted Paralysis of both recurrent laryngeal nerves results in the cessation of the respiratory movements, but if the vocal cords are immobilized sufficiently close to each other phonatory movements can still occur

Normally the most important phenomena of the phonatory movements of the vocal cords are of two kinds which can be seen by means of a high-speed film or simpler and thus more practical by the aid of a laryngeal stroboscope. One of these phenomena concerns the amplitude of the vibrating vocal cord and is, among other things, dependent on the tonus of the cord and is normally reflected in the volume of the given tone The other one is the "glottic wave" (in German "Randkantenverschiebung") This phenomenon was first registered in the famous Bell film of 1938 but was first studied closely by Svend Smith in the mid fifties. He showed in brilliant model experiments that a glottic wave could be obtained only if the superficial layer and the large mass of the vibrating body were of different consistency At phonation in normal speech tone, the musculature in the healthy vocal cord is more or less actively conctracted which, of course, does not go for surrounding tissues, and a glottic wave can also be seen. If phonation is made at high frequency especially in falsetto the musculature of the vocal cord is only slightly contracted, or not at all. From a vibratory point of view the vocal cord then consists of a homogeneous mass which has a passive tonus, as stressed by Damsté (1968), i e. the attachments of the vocal cord are removed from each other by contraction of the cricothyroid muscle, and a glottic wave cannot be seen

Loss of the cricothyroid function causes small qualitative changes in the mobility of the vocal cords, but it has been known for a long time that if paralysis of the recurrent laryngeal nerve develops, the glottic wave of the homolateral vocal cord disappears, and it seems reasonable to assume that this is because the vocal cord loses its own tonus and becomes homogeneous from a vibratory point of view Another phenomenon which is also found in paralysis of the recurrent laryngeal nerve is a side difference in amplitude where the paralysed vocal cord can show a stronger as well as a weaker deflexion than the healthy one

It is, however the loss of the glottic wave

and, especially the judgment of the return of it which belong to the interesting things in paralysis of the recurrent laryngeal nerve. It is well known and is probably best described by Schönhärl in his book on stroboscopy of 1960 that the return of the glottic wave is the first sign of a recovering paralysis of the recurrent laryngeal nerve. It is thus usually possible to see in stroboscopic light a glottic wave one or a few weeks before mobility of the cord can be seen in ordinary light. Undoubtedly it is true that if a recurrent paralysis recovers completely the return of the glottic wave is the first sign, but the opposite, viz. that a returning glottic wave also signifies the return of abduction is not absolutely certain. If a recurrent laryngeal nerve is injured seriously enough to degenerate, there is from a neurophysiological point of view no reason to assume that on regeneration the nerve fibres are going to reinnervate the same muscle fibres or the same muscles as before. On the contrary there are good reasons to suppose that reinnervation will occur randomly so that in one and the same muscle there will be mixed nerve fibres which normally cause contraction at inspiration, i.e. of the abducting muscle, and others which normally cause contraction at expiration, i.e. have an adducting function. This mixed innervation has been shown electromyographically by Hiroto *et al.* (1968) and is presumably what Faaborg-Andersen (1964) had observed when he called attention to the fact that many vocal cords immobilized by paralysis of the recurrent laryngeal nerves still showed reinnervation potentials. However such an irregular reinnervation will also give rise to at least some muscular tonus, and this is probably the explanation of what can occasionally be seen when a patient with paralysis of a recurrent laryngeal nerve reveals a discrete glottic wave for a period of up to several weeks, but without the expected increasing mobility seen in ordinary light. On such occasions innervation has returned, but function has not, and it seems likely that a relatively considerable number of patients with non-recovering paralysis of recurrent laryngeal nerves consist of such cases. It should therefore be correct to entertain a cautious optimism if you in a patient with a recurrent nerve paralysis find a returning glottic wave in the paretic vocal cord, but you cannot at the sight of such a glottic wave abandon additional control of the mobility of the vocal cord and the patient's voice until further assurance of the final result has been gained, as the glottic wave can only give information of the tonus in the muscle of the very vocal cord at phonation. It is not at all possible to draw conclusions as to the innervation of the same muscle at inspiration, nor as to other laryngeal muscles as a whole.

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In paresis of the recurrent laryngeal nerve the homolateral vocal cord cannot adduct or abduct, but some of the phonatory movements can still be seen in stroboscopic light or on the high-speed film A discussion of the conclusion which can, and also of those which cannot be drawn from the return of the missing phonatory movement of the paretic vocal cord, the glottic wave is presented.

The larynx has a number of different functions of which the respiratory and the phonatory ones are the most important It is essential for respiration that the vocal cords can be abducted in order to be out of the way for the air stream and that they can be adducted in coughing. For phonation, the vocal cords have to be adducted Paralysis of both recurrent laryngeal nerves results in the cessation of the respiratory movements, but if the vocal cords are immobilized sufficiently close to each other phonatory movements can still occur

Normally the most important phenomena of the phonatory movements of the vocal cords are of two kinds which can be seen by means of a high-speed film or simpler and thus more practical by the aid of a laryngeal stroboscope One of these phenomena concerns the amplitude of the vibrating vocal cord and is, among other things, dependent on the tonus of the cord and is normally reflected in the volume of the given tone The other one is the glottic wave" (in German Randkantenverschiebung") This phenomenon was first registered in the famous Bell film of 1938 but was first studied closely by Svend Smith in the mid fifties. He showed in brilliant model experiments that a glottic wave could be obtain only if the superficial layer and the large m of the vibrating body were of different c sistency At phonation in normal speech t the musculature in the healthy vocal cord more or less actively contracted which, course does not go for surrounding tiss and a glottic wave can also be seen If ph ation is made at high frequency especially falsetto the musculature of the vocal cord only slightly contracted, or not at all. From vibratory point of view the vocal cord th consists of a homogeneous mass which has passive tonus as stressed by Damsté (196 i e. the attachments of the vocal cord are moved from each other by contraction of t cricothyroid muscle, and a glottic wave can be seen.

Loss of the cricothyroid function cau small qualitative changes in the mobility the vocal cords, but it has been known for long time that if paralysis of the recurr laryngeal nerve develops, the glottic wave the homolateral vocal cord disappears, and seems reasonable to assume that this is b cause the vocal cord loses its own tonus a becomes homogeneous from a vibratory po of view Another phenomenon which is al found in paralysis of the recurrent laryng nerve is a side difference in amplitude, whe the paralysed vocal cord can show a strong as well as a weaker deflexion than the healt one.

It is, however the loss of the glottic wa

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ELECTROMYOGRAPHY IN VOCAL-CORD PARESES

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A recently developed electromyographic recording technique usually permitting identification of about 20 individual motor-unit potentials from each vocal muscle has been utilized in some cases of traumatic recurrent nerve pareses. As an adjunct to the ordinary routine clinical examinations, this method seems to be useful in cases in which prognostic evaluations are uncertain owing to difficulties in assessing the lesion present.

In the course of a series of investigations of the electromyographic activity in vocal-cord pareses it proved to be difficult in many cases to determine to what extent the recorded motor-unit potentials deviated from normal, since no reliable data were available on the activity pattern in the normal vocal muscle. It has previously only been possible to identify a small number of individual motor-unit potentials from each muscle. In a paper to be published (Knutsson *et al.* in press) a recently developed method usually permitting identification of 20 motor-unit potentials from each muscle has been described and data presented on the electromyographic activity in the normal vocal muscle, as based on an analysis of the shape, duration and amplitude of 469 motor-unit potentials from 18 muscles.

The method has now been applied in examinations of patients with various types of disturbed vocal-cord motility, among them seven cases of traumatic recurrent-nerve lesions, and as will appear from the three illustrative cases presented below, it has been possible by means of this new technique and the data recently assembled on the normal electromyographic pattern, to assess significant deviations relevant for prognostic evaluations.

Since a full description of the technique employed will be presented in the paper now in press, only a few principal details will be given below.

For the recordings, a conventional EMG needle is used which is inserted through the cricothyroid membrane at the midline, just above the cricoid cartilage. The vocal cords are brought into an adducted position by requesting the patient to hold his breath after an inspiration, and the needle is then further advanced after being angled medially upwards and slightly laterally. As soon as the electrode makes contact with the vocal cord change in the electrical resistance at the tip is displayed on the oscilloscope screen. The needle is then pushed approximately 1 cm further into the muscle and the recordings performed under gradual withdrawal and rotation of the electrode.

Routinely try to record some 20 of the motor unit potentials set up spontaneously during quiet breathing (Weddell *et al.*, 1944), and these potentials are photographed for subsequent analysis. The activity during deglutition and phonation is also recorded at two or three different points in each muscle. In normal subjects, these activations result in typical interference pattern which in cases of extensive denervation undergoes characteristic changes (Faaborg-Andersen, 1957).

The recordings are performed under local anaesthesia of the skin at the site of needle insertion and of the subglottic mucosa and can usually be terminated in about 15 minutes. During the first hours after the examination the patients may experience a slight irritation in the larynx and develop some hoarseness, which, however, invariably subsided within 24 hours. No other untoward effects were observed in about 50 examinations so far performed.

Case I was a 26-year-old man, operated on for a branchiogenous cyst of atypical localization in the neck. The recurrent nerve had to be

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PALATAL MUSCLE ACTIVITY AND VELAR MOVEMENTS IN SPEECH

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This study was made to provide electromyographic information on the discrete activity of the individual palatal muscles in speech and some non-speech activities. Specially designed monopolar needle electrodes were inserted transnasally and very thin wire electrodes transorally into the levator tensor superior constrictor and palatoglossus, palatopharyngeus muscles, respectively Cineradiography was carried out during EMG-recordings from the levator and palatoglossus muscles. Levator activity was closely related to velopharyngeal closure and palatoglossus activity to lowering of the velum. Some intensity and time relationship are analysed and the results are presented.

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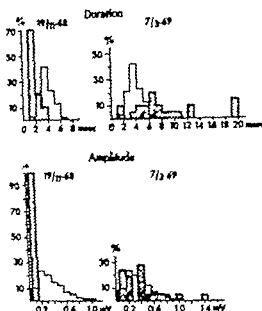


Fig. 3. Duration and amplitude distribution of motor unit potentials recorded from vocal muscle in Case 3 (hatched columns) on two occasions, showing different stages of motor disturbances, as compared with corresponding data from the normal material (white columns).

were denervation potentials. In this case it was anyhow possible to establish that a partial denervation had occurred since there was evidence of regeneration. As appears from the histogram, more than 30 % of the potentials have a duration exceeding 6 msec: this incidence is much higher than in the normal material. All these potentials except one as well as some potentials of shorter duration, totalling 40 % were polyphasic and of relatively low amplitude. The incidence of polyphasic potentials in the normal material is only 5 %, in single individual cases up to 15 %. Judging from the electromyographic recordings, re-innervation was in progress, and the prognosis should thus be favourable. Ten weeks after operation, i. e. ter another six weeks, the vocal cord had in f t resumed normal motility the voice being in th patient's opinion of the same strength as pre-operatively.

Case 3 illustrates a considerably more delayed re-innervation in a 65-year-old patient who due to disturbed heart rhythm after a myocardial infarction had had a pacemaker applied and on this occasion, in an emergency situation, the left vagus nerve was apparently injured. Owing to his poor general condition it was not observed that he was hoarse until two months after operation, and laryngoscopy was not performed until after another seven months. The left vocal cord was then found to be immobile in the paramedian position. EMG recordings were performed from the paretic muscle, and the duration and amplitude of the potentials found are plotted on the left-hand side in Fig. 3. A few single motor-unit potentials were set up during deglutition, but most of the potentials had features characteristic of fibrillation potentials. The electromyogram thus disclosed a pronounced denervation, but no total interruption of the nerve. Four months later the vocal cord was still paralytic, but the electromyogram was then quite different, as is evident from the histograms on the right hand side of Fig. 3. The amplitude distribution was now similar to that in the normal material, but most of the potentials had a duration far above normal values. Although the incidence of polyphasic potentials was not significantly higher than in the normal material, the increase in duration was considered indicative of progressive re-innervation, an assumption that was confirmed a month later when the clinical examination disclosed incipient motility of the vocal cords, and the voice had also improved.

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DISCUSSION

F. Peytz and H. Rasmussen: In the Finsen Institute, Copenhagen, we have performed studies with stimulation of the vagus nerve and its

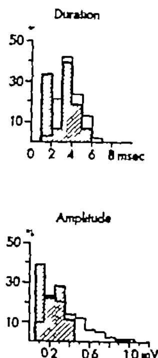


Fig. 1 Duration and amplitude distribution of motor unit potentials recorded from vocal muscle in Case 1 (hatched columns) as compared with corresponding data from the normal material (white columns).

dissected free on the left side. Although no lesion was observed at operation the left vocal cord was postoperatively immobile in the paramedian position and was still paralytic three weeks after operation. EMG recordings from this period disclosed only diffuse potentials of low amplitude, indicating pick up of activity from nearby muscles, e. g the cricothyroid. As judged from laryngoscopic inspection, the vocal cord had resumed normal motility four weeks later and the voice appeared to be normal At this time, the electromyographic activity during deglutition showed no interference pattern and only sparse motor unit potentials Eighteen potentials were identified, the duration and amplitude distribution of which appears from the histograms in Fig. 1 (hatched columns) in which for comparison also corresponding data on the 469 potentials from 18 previously analysed normal muscles are included (white columns) In this case the relative number of potentials of a duration less than 2 msec. is considerably larger than in the normal material as is also the incidence of potentials of an amplitude below 0 15 mV

All low amplitude potentials were of short duration although this does not appear from the histograms. They should thus be regarded as fibrillation potentials, indicating a denervation Since, however a large proportion of the potentials fall within normal limits both as regards duration and amplitude, the interruption of the nerve should only be partial and prognostically full recovery can be expected

Case 2 was a 50-year-old man with an immobile left vocal cord following strumectomy due to an atoxic adenoma. Four weeks after operation the vocal cord was still immobile. EMG recordings performed at this time disclosed that only a few single motor-unit potentials were set up on activation by deglutition. The histograms in Fig. 2 illustrate the duration and amplitude distribution of 20 identified potentials as compared with normal values. As seen 15 % of the potentials have a duration of 2 msec. or less. In the normal material, the incidence of such brief potentials is much lower but since single individual normal muscles may occasionally display a similar incidence (Knutsson *et al* in press) it is not justifiable to draw the conclusion that these brief potentials

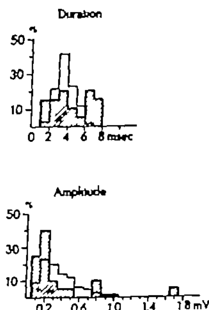


Fig. 2 Duration and amplitude distribution of motor unit potentials recorded from vocal muscle in Case (hatched columns) as compared with corresponding data from the normal material (white columns).

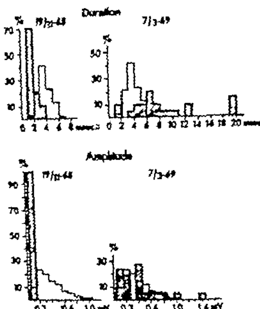


Fig. 3. Duration and amplitude distribution of motor unit potentials recorded from vocal muscle in Case 3 (hatched columns) on two occasions, showing different stages of motor disturbances, as compared with corresponding data from the normal material (white columns).

were denervation potentials. In this case it was anyhow possible to establish that a partial denervation had occurred since there was evidence of regeneration. As appears from the histogram, more than 30 % of the potentials have a duration exceeding 6 msec; this incidence is much higher than in the normal material. All these potentials except one as well as some potentials of shorter duration, totalling 40 % were polyphasic and of relatively low amplitude. The incidence of polyphasic potentials in the normal material is only 5 %, in single individual cases up to 15 %. Judging from the electromyographic recordings, re-innervation was in progress, and the prognosis should thus be favourable. Ten weeks after operation, i.e. [illegible] another six weeks, the vocal cord had in [illegible] resumed normal motility, the voice being in the patient's opinion of the same strength as pre-operatively.

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DISCUSSION

F. Peytz and H. Rasmussen: In the Finsen Institute, Copenhagen, we have performed studies with stimulation of the vagus nerve and its

branches since 1963 The technique, which was devised in collaboration with Professor Buchthal and was published in the Danish Medical Bulletin in 1965 is briefly as follows Electrodes are inserted percutaneously and paratracheally 2.5 cm below the cricoid cartilage for stimulation of the recurrent nerve and at the same level behind the sternocleidal muscle for stimulation of the vagus nerve and in front of the vascular sheath at the level of the hyoid bone for stimulation of the superior laryngeal nerve. Electromyography is performed simultaneously with electrodes in the muscles concerned, i e. percutaneously in the cricothyroideus and by direct laryngoscopy under local or *general anaesthesia in the vocalis and in the* posterior cricoarytaenoideus muscle.

We have studied about 270 patients—some of them repeatedly and in several cases bilaterally Among the 270 patients, paresis of the recurrent nerve was present in about 100 while the remaining patients were normal or were examined for laryngeal cancer or neuromuscular disorders, or were *studied during thy*roid operations with a view to localization of the recurrent nerve About one half of the patients with paresis of the recurrent nerve were studied within the first 6 months after the occurrence of the paresis, the earliest examination being performed 4 days after the onset. The remaining cases were of longer duration the oldest case had persisted for 32 years. The two largest groups were post-strumectomy pareses and pareses of unknown aetiology Other groups were, for example, malignant lesions of the neck or lungs, and so-called central pareses.

From our studies we conclude that in paresis of a duration of up to 6 months a response of normal amplitude and with normal conduction time is suggestive of a favourable prognosis. The earlier a response is obtained and the more it approaches normal with regard to amplitude and conduction time, the better is the prognosis. However caution should be exercised in the assessment of the response as fairly wide variations seem to exist. So far our knowledge is limited, but we hope that in the study of a sufficiently large number of cases it will be possible to reveal definite prognostic signs by means of this method.

S Fex Did you do registrations also at inspiration? From a prognostic point of view it would be of value to know if what Sribodhi *et al* called "misdirected fibres" has been the reason for unphysiological re innervation, i.e. abnormal function.

S Haglund (Reply *to Fex*) *It has been pos*sible without difficulty to keep the electrod in a stable position to permit recordings from single motor units during repeated respiratory phases. In some units, the discharge frequenc was comparatively stable, whereas, in others the frequency varied with respiration. Som of these units fired only during one of the re*spiratory phases.*

Therefore, from pathological cases with sign of re innervation it does not seem possible to draw a conclusion of misdirected fibres in the way it has been done in the paper by Hiroto *et al*

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ELECTROMYOGRAPHIC STUDIES OF THE FUNCTION OF THE FACIAL MUSCLES IN DYSARTHRIA

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The EMG activity picked up by needle electrodes from six facial muscles, mainly responsible for the labial articulation, was recorded simultaneously with the speech. Through repeated detailed studies on one speech-trained subject and analytic comparison between several individuals with normal articulation, we have gained knowledge of the normal neuro-motor activity of the mimic musculature during speech. In this paper we present the common characteristics of the EMG speech pattern of normal speakers compared with that of patients with organic dysarthria.

Relatively few experimental studies have been made on the function of the facial muscles during speech. It was not until the beginning of the 1960's that a group of phoneticians at the Haskins Laboratories in New York started to use the electromyographic technique in their studies of speech to find a neuromuscular pattern for linguistic elements and speech gestures. They used mainly surface electrodes. But if we want to study simultaneously the reciprocal innervation of the muscles and the muscle co-ordination indispensable to fluent speech, it is necessary to use needle electrodes, because of the topographically complex anatomy of the muscles around the lips. Properly placed, these electrodes will give satisfactory functional separation.

Articulation disturbances caused by organic diseases in the nervous system of the speech organs, dysarthria, have so far been studied mostly clinically by subjective auditive and visual assessment and experimentally by objective spectrographic analysis. By interdisciplinary phonetical, neurophysiological and phoniatrical co-operation we have developed a method of examination and identified the particular electromyographic pattern of the individual normal-speaking person and found

ELECTRODE POSITIONS

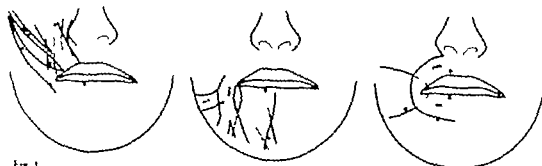


Fig. 1

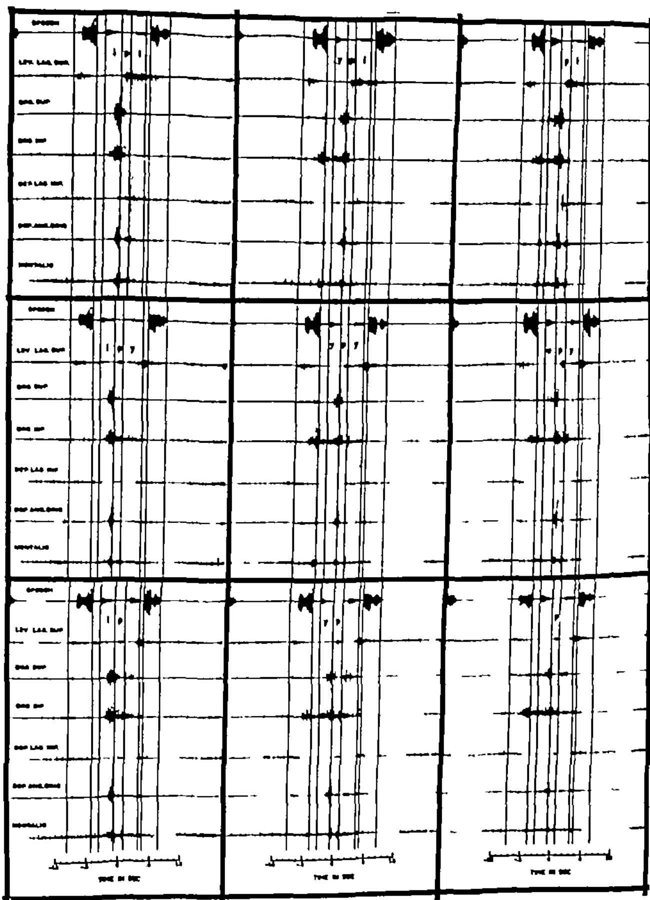


Fig. –

characteristic EMG features common to the entire normal group

Against the background of these observations we then studied the movements of lip articulation in a group of patients with Parkinson's disease and dysarthria. A comparative analysis showed that several deviations in the EMG pattern were common to this group

Fig 1 shows the electrode positions used in nearly all the studies. The investigated muscles were the levator labii (LLS), the orbicularis superior (OOS) and inferior (OOI) the depressor anguli (DAO), the depressor labii (DLI), and the mentalis (M) They were chosen in explorative studies of all the functional muscle units in the facial region. The technique used in finding the optimal needle position is described in the Proceedings of our Scandinavian Congress in Helsinki, 1966, in which the phonetic material for the movements of articulation is also presented. The EMG activity was recorded simultaneously with speech on a multi-channel tape-recorder and traced on a polygraph or an EEG apparatus.

The prerequisite for fluent speech is a well-learnt neuromuscular speech pattern. This is individual, and under standardized experimental conditions and with a suitable phonetic material it is well reproducible at repeated investigations.

Fig. 2 shows a series of V_1CV_2 (vowel–consonant–vowel) combinations placed in a constant linguistic frame. C=/p/ and the vowels, which change place throughout, are /i/ /u/ and /y/ An analysis of the EMG activity of the relevant facial muscles recorded simultaneously with speech shows the following features.

Muscle function during speech consists partly of a basic tonus, which has also been found, for instance, in chest and palate muscles and which we call speech posture partly of a manipulatory activity The initial position of the mimic muscles is influenced by a variety of factors—we smile, are sad, tense, relaxed, and so forth. The manipulatory activity is much faster and produces the different single sounds. The postural activity is found in the levator and depressor labii and the manipulatory activity mainly in the orbicularis and depressor anguli. This functional distribution is very striking and indicates that the facial muscles contain both tonic and phasic components.

At labial articulation movements the EMG tracings of the activity of the perioral muscles show normally a well co-ordinated excitation and inhibition, respectively of the different muscle groups that act synergistically or antagonistically The activity in a muscle for a particular sound depends on the position of the lips and the activity of the muscle during the preceding sound (see /i/ or /y/ after /p/ or /p/ after /y/ and /i/ respectively). The neuronal instruction to the facial muscles is, for instance different for an /i/ depending upon whether the preceding lip movement is rounded or spread. This fact gives rise to questions concerning the afferent flow of impulses. What type of muscle receptors occur? What part do skin and mucosal sensation play? Of what significance is auditive feed-back?

If muscle spindles occur they are very few and would not play any predominant part. We have started studies with masking of hearing and various types of anaesthesia of the trigeminal nerve. We are also planning to investigate patients with trigeminal neuralgia after nerve block and root section.

The EMG activity starts before the sound is heard, and this interval varies for different sounds and for the same sound in different positions, for instance for a vowel, depending on whether it is preceded by a labial or a non-labial consonant (cf. /y/ as V_1 with /i/ as V_2 after /p/). The onset of activity for a consonant is dependent of the foregoing vowel (see /p/ after /i/ /y/ and /u/ respectively). The EMG activity of a rounding or spreading movement for a vowel that is not preceded by a labial consonant starts about 200 msec. before the sound is heard, but about 80 msec. after a labial stop like /p/ The EMG activity for /p/ appears 10 to 15 msec. earlier after /i/ than after /y/ and even later after /u/ (The lip position of /u/ is very near to that of /p/)

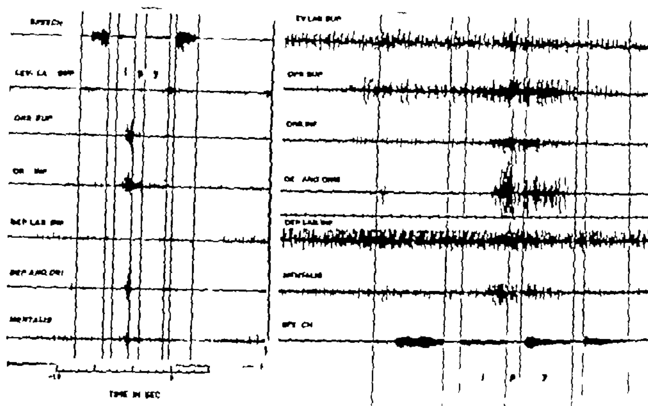


Fig 3

The implosion phase and the release phase of a normal stop consonant are very well co-ordinated *If the succeeding vowel is spread, the vowel command coincides with the release* activity which will then appear earlier

The *EMG* pattern is constant in one and *the same subject. In one of our subjects we* made at least some ten studies on different occasions with reproducible results.

Variations occur between subjects, particularly of quantitative nature and with respect to basic tonus—"speech posture"—from complete *relaxation between utterances* to continuous tonic activity on which the manipulatory activity is then superimposed in both excitation *and inhibition Studies of a group of* normal speakers have demonstrated common EMG characteristics *These then* served as material *for comparison* in *studies of patients* with organically conditioned disturbances of articulation

Fig 3 shows a comparison *between normal* articulation and dysarthria in Parkinson s disease The patient s EMG *pattern shows* a generally *markedly* increased tonus, notably in the muscles responsible for the postural activity the levator *labii and the depressor* labii. This pathological hypertonia does not allow the manipulatory excitation and inhibition activity *which is seen in the normal speaker* even at increased basic tonus.

The normally well co-ordinated and properly *balanced synergistic-antagonistic function* is upset. Not only do all the muscles function simultaneously and *inadequately* but there is *also an increase in antagonistic activity* instead of a decrease (the levator labii, which is really an /i/ muscle becomes just as active for /y/ *when it should stop functioning)*

Normally the onset activity for a sound decreases throughout the continuance of the sound, *and if a spread vowel is preceded* by a similar vowel, no new activity is seen. In the patient we find that the activity *lasts longer and that it is renewed for a similar sound* The onset activity period i e. the period by which the *EMG activity precedes the sound*, is also longer This long-lasting activity can interfere with and sometimes prevent the production of *a new sound and result* in a kind of perseveration (/ypi/ becomes /ypy/)

Normally there *is a difference of* 20 per

Fig. 4.

Fig. 5

cent in EMG activity as regards both the closing and the opening phase for /p/ and /b/ respectively With the higher intra-oral pressure at the voiceless /p/ with abducted vocal cords the lips must be closed more firmly but, in compensation the opening of the lips is easier The voiced /b/ with the glottis closed has normally a lower intra-oral pressure, the lip closure needs less muscular activity but the lip opening must be more active than for /p/ This difference is not found in patients

Fig. 4 shows a comparison of two patients One (to the left) has been ill for a short period and has only slight dysarthria. Muscle hypertonia is more marked in the other patient and lip movements are stiffer manipulatory activity is slower and becomes increasingly weaker Co-ordination, in particular is impaired The individual sounds can be produced one by one but not in the rapid sequence required in fluent speech, and so the patient s speech becomes indistinct and unintelligible.

Fig. 5 shows two EMG tracings from the same patient at an interval of six months. On the second occasion, the basic tonus has increased in all the muscles, notably in those with mainly postural function, the depressor labii and the levator labii The balance between synergists and antagonists is also further upset. Instead of reducing its activity during the closing phase for /p/ the depressor labii now acts in the opposite way

The function of the afferent mechanisms normally essential to fluent co-articulation must be disturbed in these patients. By continued studies of normal speakers and of patients, on the basis of what is already known of the pathophysiology of Parkinson s disease and from other viewpoints, we hope to obtain further data on these mechanisms.

EMG studies of the facial muscles during speech provide the phonetician with important information as a complement to acoustic phonetics. They are also of neurophysiological interest by allowing the study of a complicated muscle function which is stereotypically automated and reproducible They are, however of particularly great importance in phoniatrics as a means of studying both organic and functional disturbances in articulation.

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INFLUENCE OF THE NOSE ON THE ACOUSTIC PATTERN OF NASAL SOUNDS

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After changing the conditions in the nose on one or both sides, an attempt was made to ascertain the influence of these changes on the formation of the nasals *m* and *ng* both by auditory perception and by spectrographic methods[1]. Complete closure of one side did not cause any change in the auditory perception of the nasals. However the decrease in, or disappearance of, energy in the higher-frequency areas can be established in the sonagram. Complete closure on one side and partial closure on the opposite side cause changes as follows. As long as the lowest nasal cavity is free, the epipharyngeal-nasal cavity formant, which is apparently formed primarily in this area, remains unchanged, i.e. at 250 cps. This is the most important frequency area of the nasals. If the lowest—and only—nasal cavity is closed, the higher frequencies will be intensified, and auditory perception receives plosive characteristics; if complete closure is brought about, the nasals get corresponding plosive structure. Individual variations are very wide in the formation of the nasals.

The Finnish nasal sounds *m*, *n* and *ng* are formed by using the lip the tongue and, above all, lowered velum and nasal cavity According to the pronouncing place m can be characterized as a labial nasal, its corresponding plosives being *b* and *p* n as a dental nasal, its corresponding plosives being *d* and *t* ng as a palatal nasal, its corresponding plosives being *g* and *k*. The acoustic relationship of these is shown in Fig. 1 in which the sonagram has been presented schematically

In regard to their acoustic structure the nasals, however resemble most of all vowels, even though the vowel formants proper i.e. formants of the pharyngeal cavity and oral cavity are in a less important position. The so-called formants (F 1 F 2, F 3 F 4 etc.) are harmonics or groups of harmonics reinforced in the resonance cavities of the vocal tract.

Further it is to be observed that nasalization is rather the rule than the exception in vowels which are situated near a nasal consonant or between them (Björk, 1961 Fant, 1968). In brief the following three factors may be mentioned as the characteristic features of a more or less nasalized vowel (Fujimura, 1958):

1 Intensity growing in the area of 250 cps.
2 Intensity weakening in the area of about 500 cps.
3 Appearance of comparatively weak and diffuse components between the vowel formants in the area of 1000–2500 cps.

In the Finnish nasals the energy concentrations, the formants or components are as follows (Sovijärvi, 1959 1961 Ylppö & Sovijärvi, 1962 Kyttä, 1965

FN 1 = formant of the epihypopharyngeal cavity	200–250 cps
FN 2 = formant of the epipharyngeal cavity	1500–1600 –

Formants of the lower (inferior), middle (medius) and upper (superior) nasal passage respectively

FN 3 inf.	1950–2300 cps
FN 3 med.	2300–2700 –
FN 3 sup.	2700–3300 –
F 4	3300–3450 –

1 The sound spectrograph "Sonagraph" was used for the analysis of the physical quality of sounds. The Sonagraph was described in greater technical detail by Potter et al (1947) and Fant (1968).

According to Fant (1968) a voiced occlusive nasal (nasal murmur) is characterized by a spectrum in which F 2 is weak or absent. A *formant at approximately 250 cps generally* extending into adjacent vocalic segment pre *dominates* the spectrum but several weaker high frequency formants (not always seen in spectograms) occur one typically at 2200 cps These higher formants are generally weaker than for laterals. The bandwidths of nasal formants are generally larger than in vowel like sounds.

The vowel formants proper are of secondary importance in the nasals. F 1 is found to be 300–430 cps, F 2 500–1900 cps and F 3 1800–2600 cps. The nasal *m* lacks a third for *mant because of the bilabiality of this sound*

Being vowel formants proper F 1 and F 2 are of secondary importance in the nasals themselves, but perform a definite transition decisively influencing the acoustic pattern of the preceding and following vowels Thus, the initial *m* during the transition to the following vowel causes an upward glide of F 1 and F 2, whereas the medial m causes the opposite phe nomenon in the preceding vowel The initial *n* causes shifting of F 1 upwards, and of F 2

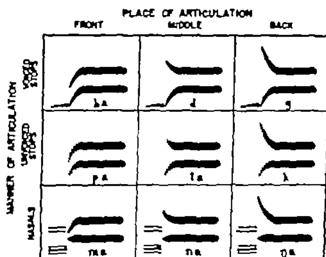


Fig. 1 Spectrographic patterns illustrating the transition cues for the stop and nasal consonants in the initial position with the vowel a The dotted portions in the second row indicate the presence of noise (aspiration) in the place of harmonics. After Liberman (1957).

downwards, if the F 2 of the vowel that follows *n permits this When n is in* medial position, the F 1 of the preceding vowel falls and F 2 rises subject to the above condition as regards F 2 In the case of *ng* approximately the same phenomenon occurs as in the medial *n* but is often less distinct because the F 1 area is broader than above. Thus, if one covers the nasal sound in the sonagram, it is possible, in the transition phase of the F 1 and F 2 of the preceding or following vowel, to say which of the nasals is concerned in each case. F 3 is not affected by the proximity of a nasal (Figs. 1 and 2)

In addition to the formant transition and formant resonances playing and essential part *in the acoustic identifiability of the nasals, there* is also another phenomenon, characteristic of the nasals alone and directly contrasted with the formant resonances. This is the anti-resonance produced by the oral cavity Fant (1960) stated. "The effect of the mouth cavity as a side chamber shunting the sound transmission through the pharynx nose system, is to cause a shift of resonance frequencies and to introduce anti resonances. It has been verified by supplementary analog experiments that an increase of the coupling area to the mouth cavity as in the case of an incomplete lowering of the velum or a lowered tongue position, shifting the mouth cavity anti-resonance up to 100 cps, causes a neutralization of the 1000 cps nasal formant" Anti-resonance can be observed as gaps" which become very prominent, especially in sections (Fig. 2) By changing the conditions in the nose (e g with a piece of cotton dipped into sodium chloride), it is at first seen that complete closure on one side does not cause a change in the auditory perception. In the sonagram one observes a general weak ening of energy in the higher frequencies (Fig. 3 B) Thus, even bad septum deviations on one side, hypertrophic conchae or polypi have no considerable influence upon the acoustic pattern of the nasal.

If after this, changes are caused in the nose passa

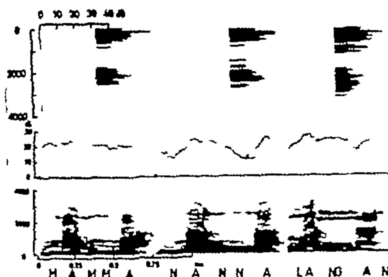


Fig. 2. Spectrographic analysis of the anti-resonance found in nasals and appearing in the sections as "gaps". It is seen that the gap is broadest in the labial *m*, narrower in the apico-dental *n*, and narrowest in the dorso-velar *ng*

completely closed—it is observed that the glotto-pharyngeal-nose cavity formant remains at 250 cps as long as the lowest nose passage is free, and even becomes stronger if there is an obstacle in the middle or upper passage of the nose. The resonance of the upper nose passages is either missing or becomes weaker, more diffuse and similar to noise in the sonagram (Fig. 3 D). The phenomenon is opposite if the lowest passage of the nose is closed (Fig. 3 E). If one further continues the experiments with closure of the nose, so that the nose pas-

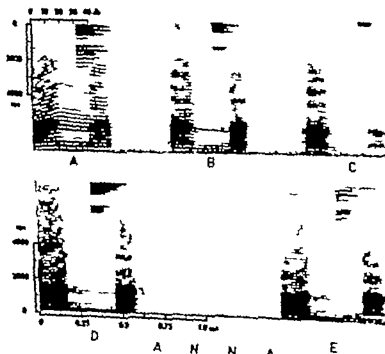


Fig. 3. Spectrographic analysis of the nasal sound *n*. A, the nose is completely open. B, one side of the nose is closed. C, the nose is completely closed. D, one side of the nose and the upper passages of the other side are closed. E, one side of the nose and the lowest passage of the other side are closed

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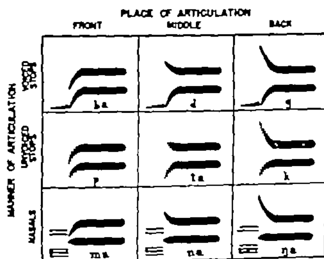


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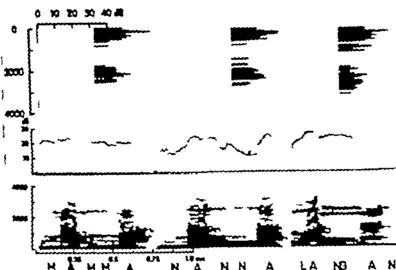


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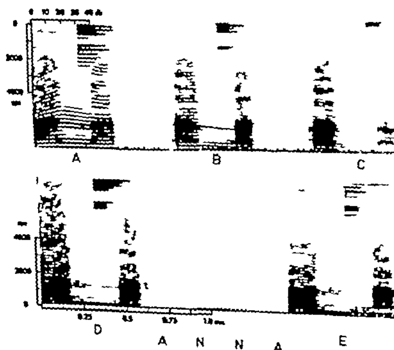


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sages are otherwise free, but the nostrils are closed it is observed that FN 1 formant rises up to 350 cps. If the obstacle is pushed deeper into the nose, it is observed that this formant rises further and when the midway to the septum has been reached, i e approximately 4 cm from the nostrils the formant rises up to 500–1000 cps, which is the same level as the anti resonance has. The nasalization stops and the nasal consonant in question changes into some other sound In some cases, it may start to resemble the preceding or subsequent vowel or—which is most common—*m* gets the acoustic structure of *b* or *p* *n* that of *d* or t, and *ng* that of *g* or *k* as it was somehow to be expected and as was discussed in the beginning of this presentation when listing the corresponding plosives (Fig 1)

In this connection, attempts have been made to ascertain the influence of the side cavities of the nose especially the most accessible of these, the cheek cavities, upon the nasalization After filling first one of the cheek cavities and then the other with radio-opaque material (Dinosil) the consistency of which is comparatively thick, sonagrams were recorded, but no considerable changes were observed It is apparent that the oral and nasal stress needed for normal speech is so small that hardly any side cavity resonance appears the situation is different in singing or even perhaps in reciting, because the performer needs then a larger soundboard, and co-operation of the side cavities is necessary

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PROMINENT EARS

A TECHNIQUE FOR PLASTIC CORRECTION

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A technique for correction of congenitally prominent ears is described. The ear is brought into the natural position in relation to the head, and the anthelix and crura are reconstructed so that they appear well formed. The method utilizes the known spontaneous bending tendency of the auricular cartilage following scratching of the anterior surface of the cartilage. To bring the lower part of the ear and the lobe into the natural position, thinning of the cauda helicis and antitragus cartilage is used. The ear is kept in the desired position by using mattress sutures. A check-up of patients operated on by this method was performed.

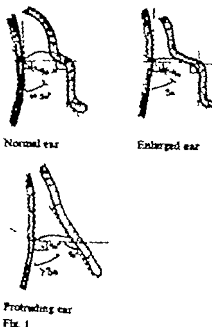
Prominent ears is a congenital deformity which is often the cause of teasing, a constant source of humiliation and always an occasion for hints. In many cases, this deformity gives the physiognomy a queer ridiculous expression, which may now and then give rise to psychic problems. Embryologically prominent ears is a deformity caused by a evolutional anomaly of the mandibular arch and the hyoid arch of the first branchial groove In rare cases, the cause can be an intra-uterine lesion, but in such cases the deformity is usually unilateral.

The external ear is developed about the sixth embryonic week and reaches its final shape about the third embryonic month. However the folding of the anthelix and crura anthelica is not accomplished until the sixth embryonic month.

The angle between the normally placed external ear and the skull (cephaloscaphal angle) is about 30 Seen from behind the angle between the concha and the skull is about 90 and will be almost the same for a normal ear and a prominent ear In normal ears, the angle between the concha and scapha is about 90° while in protruding ears this angle is greater than 90 (Fig. 1)

Review of Literature

In the literature numerous methods of correcting prominent ears are reported. Several of these are only of historical interest to-day Some methods describe a conservative way of correcting the deformity Tying the external ear to the skull for a certain period of time, and gluing the ear to the planum mastoideum have been



Normal ear

Enlarged ear

Protruding ear

Fig. 1

suggested. These methods proved useless, due to the elasticity of the ear cartilage which remains unaltered in spite of a temporary change in position

The first surgical correction of outstanding ears was described by Dieffenbach in 1845 He made an excision of the skin from the back of the external ear followed by suture of the cartilage to the periosteum of the mastoid. In 1881 Ely described a method with excision of the skin and cartilage through the entire thickness of the ear leaving a scar on the anterior surface of the auricle A similar procedure was advised by Fishman & Fishman in 1946 To avoid scarring, Keen suggested in 1890 excision of the cartilage without cutting the skin on the anterior aspect of the ear During the following years, several surgical procedures were described all with excision or incision of the cartilage, to break the elasticity of the ear cartilage (Monks, 1891 Haug, 1894 Joseph, 1896 Morestin, 1903 Goldstein, 1908 Kolle 1911 Gersuny 1903 Payn 1906 Ruttin, 1910)

All procedures on the cartilage were performed in the cephaloconchal angle in an attempt to reduce the angle and so bring the external ear nearer to the head without changing the anatomy of the ear In many cases the cosmetic result was not very satisfactory as the ear often came unnaturally near the head and the postauricular sulcus was not infrequently completely obliterated. In 1910 Luckett reported that these operations did not give a permanently good result, and that the normal anatomy of the ear was not reconstructed. Luckett realized that most outstanding ears were caused by a too large scaphoconchal angle because of a missing or badly developed anthelix. The conchal cavity continues into the scaphal fold without being divided by the anthelix fold Luckett used excision of a crescent shaped piece of cartilage where he wanted the new anthelix to appear The position of the ear was maintained by sutures through the perichondrium In spite of the fact that many new surgical procedures have subsequently been described the surgical principle utilized by Luckett is still the basis of most of the surgical methods of to-day A disadvantage which the method of Luckett and its subsequent modifications have in common is that the outcome is often an unnaturally sharp and edged anthelix. To avoid this disadvantage, Brown (1938) suggested to thin the cartilage from behind along the wanted anthelix. In 1947 Pierce et al. suggested 8–10 parallel incisions from behind, almost through the cartilage. Stenström (1963, 1966) described an important observation, viz. that cartilage spontaneously bends in the opposite direction of a scratched surface. The author utilized this observation in his operation for outstanding ears, using a superficial scratching on the anterior aspect of the cartilage to obtain a soft, shapely anthelix. Apart from ear bandage no fixation of the ear was applied. The observation of Stenström is used in the operative procedure described below

Operative Technique

Sterile cleaning of the external ear and its surroundings is used according to the normal surgical principles. When the ear is pushed back against the head, the normal anatomical details can be seen, so that a marking with dye can be made where the new anthelix and crus anthelicis inferior is desired (Fig 2) Patients with protruding ears often reveal, in addition to the missing or slightly developed anthelix, a large conchal cavity with a high conchal wall. Therefore it is often necessary to place the coming anthelix someway down in the conchal cavity especially at the most distal part. A skin incision is made on the posterior aspect along the coming anthelix fold The cartilage is separated to the free helix edge, and great care is taken to free around the cauda helicis and antitragus. Bleeding vessels are clamped, but the clamps can be removed again after a short while Only on rare occasions is it necessary to ligate a bleeding vessel, and so far we have not seen haematomata which had to be treated. Through the fissura antitragohelicina it is easy to gain access to the anterior aspect

of the cartilage, and subcutaneous undermining is carried out along the marked anthelix and crura folds. The anterior aspect of the auricular cartilage is now scratched with a special scratching instrument (Fig. 3). The scratching must not be too deep but has to be continued until the ear spontaneously folds backwards. The scratched area must be 0.5–0.75 cm wide, deepest in the midline and should be continued as far as possible out into the helix fold, to obtain a soft natural-looking passage. The correct position of the ear is often prevented by a considerable thickness of the cauda helicis and the most posterior part of the antitragus. Thinning of these two cartilage areas from behind should therefore always be performed. The ear is kept in the desired position by four mattress sutures, the upper one placed in the triangular fossa, the other ones in the conchal cavity (Fig. 4). A 2–0 silk suture is inserted from the front and brought back through the skin and cartilage, in front of the anthelix fold. On the posterior aspect, a loop of the suture catches the cartilage behind the anthelix fold, so that the suture in the loop is placed subcutaneously on the front side of the cartilage. The course of the suture is best illustrated in the diagram shown in Fig. 5. When all the sutures are placed, they are tied over small gauze rolls on the front side of the ear. By means of the mattress sutures it is possible to place the ear in the desired position. The mattress sutures are left untied until the retro-auricular wound is sutured with fine chrom catgut. These sutures in the skin have not given rise to any complications. A wet cotton dressing (physiological saline) is placed in the scaphal fold, and finally a compressing bandage is placed on the ear. After 10 days, the bandage and the mattress sutures are removed, and a new compressing bandage is then used for another 10 days. This bandage is removed by the patient himself and the patient uses for another 21 days a light stockinette bandage during the night. Mattress sutures caused no complications and at subsequent check-ups there were no visible signs of the



Fig. 2. Marking of the desired new anthelix and crus anthelicis inferior.



Fig. 3. The specially designed scratching instrument. One for the right ear and one for the left ear.



Fig. 4 Showing the four mattress sutures in place

sutures. None of the patients received prophylactic antibiotics.

The operation was performed under general anaesthesia in young children, while only local infiltration anaesthesia was employed in older children and adults. However for haemostatic reasons local infiltration of the ear with 1 % Lidocaine with noradrenaline was used in all cases.

Check up Examination

The operative procedure described has been used by the author in the Department of Otolaryngology the University Hospital of Aarhus, Denmark, since 1967 The patients subjected to operation during 1967 and 1968 have been called in for check up During this period the same surgeon operated 105 ears in 55 patients. Of the operated ears, 84 % were re-examined 26 to 5 months (average 16 months) after the operation There were 24 girls and 20 boys, whose ages ranged from 5 to 21 years one patient was 31 years old and the average age was 11 years. In six patients, only one ear was operated on Of the re-examined patients, 65 % knew of one or more family members who had outstanding ears. In 45 of the 55 patients, a pure-tone audiogram was recorded pre-operatively Normal hearing was present in 42. A slight conductive low-tone loss was found in three. Two of these patients had fairly large adenoids.

All the patients subjected to operation were very satisfied with the result of the correction and some of the children had improved psychically after having had their ears corrected. The check-up showed that 85 % of the patients now had normally placed and anatomically correct looking ears. One patient in whom both ears had been operated on revealed an outstanding right ear at the check up again placed as before the operation. In another patient, both ears showed an outfalling tendency of the upper helix edge The remaining 11 patients were found to have well-placed ears, but the anthelix was more marked or irregular than a normal looking ear Undoubtedly the cause was a too deep and narrow scratching of the cartilage In addition, these patients had ears with a hard inelastic cartilage Reconstruction of the crus inferior anthelicis was performed only in some of the patients. However it is also of great importance

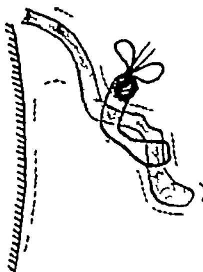


Fig. 5 Mattress sutures tied over gauze rolls.

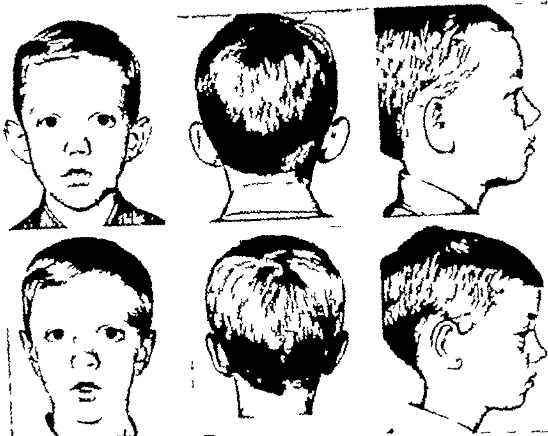


Fig. 6 The upper pictures showing the patient before operation and the lower ones after the operations.

to make a scratching of the inferior crus. The scratching here must be deeper and narrower than the scratching of the crus anthelicis superior. The cephaloscaphal angle was measured before and after the operation in all the patients. Postoperatively the angle was considerably decreased in all cases, except in the aforementioned patient with recurrence. In all cases, the angle was found to be much enlarged before the operation, but only a few revealed postoperative angle of about 30°, which is usual for a normally placed ear. The reason for this is undoubtedly that outstanding ears are generally relatively large and often combined with a considerably enlarged conchal cavity (Fig. 1).

It is usually stated that the shape of the external ear becomes permanent at about the age of 5 years, but its growth has not terminated at that time. All investigators agree that surgical procedures on the external ear does not depress normal and continued growth, and they also agree that outstanding ears should be corrected before the patient start school, i. e. at the age of 5–7 years.

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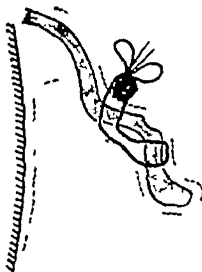


Fig. 5 Mattress sutures tied over gauze rolls.

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QUANTITATIVE ANALYSIS OF LANGUAGE PRODUCTION IN PATIENTS WITH DOWN'S SYNDROME

O Bentzen and O Nielsen

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The language in persons with Down's syndrome was analysed by two methods: electro-mechanical counting of the letters and statistical counting of letter and words by a computer. Studies based on these methods were performed on the spoken language of a pair of twins 13 years old, one twin being a boy with Down's syndrome

A main factor in the rehabilitation of deaf and hard-of-hearing children is the level of language development. In individual training and therapy as well as in the investigation of methods, a measure of language development is greatly needed (Bentzen & Willemoes, 1961)

To meet this need, a method of quantitative analysis of individual language production has been developed. This method—called quick check analysis (QCA)—meets the requirements of being both simple and quickly performed. In the following, data collected by this method have been analysed by means of a computer permitting a more detailed analysis of the language

QUICK CHECK ANALYSIS

Principle The written or spoken linguistic production of the person examined is typed on a specially constructed typewriter which, at the same time tabulates the occurrence of the smallest units in written language, i.e. the letters of the alphabet.

Method. A black-and white line drawing, illustrating a family scene in a garden, is used as a test picture This picture is shown to the person under test, who is requested to describe the picture, and the description is recorded on a tape recorder A two-minute period of this recorded description is then transcribed on the special typewriter

Apparatus An ordinary typewriter has been altered to provide an electric contact for each key including the space bar and *shift* key Striking a key closes its contact and causes an electrical impulse to advance to the corresponding counter

Analysis. Another method of analysis of speech production using the examined patient's description of a test picture was employed by Stone *et al* (1961) but their analysis of the descriptions was based on speech intelligibility and voice quality In our work, the analysis is based solely on the symbolic character of the language sample as revealed by numerical analysis of the number of words produced per minute, the average length of the words, the number of nouns, and the number of consonants produced.

Normal Standards

The linguistic production of ∠30 normal subjects aged from 4 to 80 years was recorded and analysed to provide a basis of comparison with patients.

This study was carried out with the support of Den almindelige danske Vaedenlaegefond

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QUANTITATIVE ANALYSIS OF LANGUAGE PRODUCTION IN PATIENTS WITH DOWN'S SYNDROME

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The language in persons with Down's syndrome was analysed by two methods: electro-mechanical counting of the letters and statistical counting of letters and words by a computer. Studies based on these methods were performed on the spoken language of a pair of twins 13 years old, one twin being a boy with Down's syndrome.

A main factor in the rehabilitation of deaf and hard-of-hearing children is the level of language development. In individual training and therapy as well as in the investigation of methods, a measure of language development is greatly needed (Bentzen & Willemoes, 1961).

To meet this need, a method of quantitative analysis of individual language production has been developed. This method—called quick check analysis (QCA)—meets the requirements of being both simple and quickly performed. In the following, data collected by this method have been analysed by means of a computer permitting a more detailed analysis of the language.

QUICK CHECK ANALYSIS

Principle. The written or spoken linguistic production of the person examined is typed on a specially constructed typewriter which, at the same time, tabulates the occurrence of the smallest units in written language, i.e. the letters of the alphabet.

This study was carried out with the support of Den almindelige danske Vaeleselsabsfond.

Method. A black-and-white line drawing, illustrating a family scene in a garden, is used as a test picture. This picture is shown to the person under test, who is requested to describe the picture, and the description is recorded on a tape recorder. A two-minute period of this recorded description is then transcribed on the special typewriter.

Apparatus. An ordinary typewriter has been altered to provide an electric contact for each key, including the space bar and shift key. Striking a key closes its contact and causes an electrical impulse to advance to the corresponding counter.

Analysis. Another method of analysis of speech production using the examined patient's description of a test picture was employed by Stone *et al.* (1961), but their analysis of the descriptions was based on speech intelligibility and voice quality. In our work, the analysis is based solely on the symbolic character of the language sample as revealed by numerical analysis of the number of words produced per minute, the average length of the words, the number of nouns, and the number of consonants produced.

Normal Standards

The linguistic production of 250 normal subjects aged from 4 to 80 years was recorded and analysed, to provide a basis of comparison with patients.

Table 1 *Analysis of the speech production of three groups of subjects children adults and elderly subjects over 65 years of age*

Group	n	Words/ min	Average length	Percentages Nouns	Conso- nants
Small children	50	43	3.50	30.2	60.6
School children	50	65	3.55	_3 1	60 8
University students	50	10	3.91	_3 9	61_
Nurses	50	101	3.89	4.8	60.8
Old people	50	71	3 64	~0.8	60.7

Description of Test Picture by Normal Subjects (in Danish)

It was demonstrated as illustrated in Table 1 that language production per unit of time is greatest in adults less in the aged and least in children The same tendency is seen in the average length of words, whereas the frequency of nouns decreases with increasing age

This method using electro-mechanical counting of basic letter units in the words of a patient s description of a picture was similarly applied to written language An example listing differences in several languages is shown in Table 2 in which the results are based on the same text translated into six languages.

The difference between the results in the Danish and the English language should be noted as the analysis of the language of the patients with Down s syndrome is based on the English language

Table 2. *Numerical analysis of written language based on the number of words their average length and the percentage of consonants occurring in six translations of the same text*

Language	Number of words	Average word length	Consonant percentage
German	99	5 _3	61 0
Danish	75	4 81	61 1
French	~90	4 63	58_
Swedish	311	4 46	62.0
Dutch	333	4 4	57_
English	3_	4 04	55 7

It may be asked whether or not word production average word length, and the percentage of nouns will be sufficient to characterize the quality of the language in general. To answer this question, the available test material was analysed by another method based on the principles of statistical linguistics, using an electronic computer A comparison of the results indicated that only very little additional information is derived from the use of the more complicated statistical method.

COMPUTER ANALYSIS

Principle The language sample (either written or spoken) from each person examined is statistically analysed to produce the following information.

a A *measure* of the amount of *information* in the sample

The information content is measured indirectly through a determination of the uncertainty of the receiver of the language sample s content, the message This uncertainty consists in a determination of the probability of the occurrence of the following word in the text. As an example a sample phrase beginning with "Mary had a little will lead to an extremely high probability (or insignificant uncertainty) that the following word will be lamb" As a second example the symbols "Z E B-R" will, with a very great probability value be followed by the symbol "A"

The formal concept of uncertainty which has been used is the *entropy* concept as stated in the fundamental works on information theory by Shannon (1948)

The numerical value of entropy is chosen in such a way that large entropy values correspond to great uncertainty so that an entropy value of zero corresponds to certainty In the foregoing examples, the entropy values of "lamb and A approach zero. Entropy is thus the reciprocal of the probability of occurrence.

Entropy values for a given sample provide a valuable characteristic when used together with the other objective and subjective measures. A low-entropy message will be monotonous, probably with a very limited vocabulary and with the frequent use of clichés of no informative value. A high-entropy message will be very changeable, probably with a voluminous vocabulary Extremely high values of entropy may indicate messages which are not too easily grasped On the other hand, high entropy values may indicate a lack of content, as in a nonsense poem, or the remark of the Mad Hatter in Alice in Wonderland: "Like a tea tray in the sky If it is our experience that "sky may appear in this connexion, then anything may appear so that our uncertainty and, thus, the entropy value will increase rapidly

b A *vocabulary* which gives the numerical tabulation of the frequencies of occurrence of all words appearing in the message

Apparatus These analyses were performed with the use of the computer system at the computing centre at Aarhus University The programmes were worked out at the Institute of Statistics and Data Processing of the Aarhus School of Economics and Modern Languages.

Analysis In a previous study the speech production of a 65-year-old woman and a 12 year-old boy (with an IQ of 170) were compared with an excerpt from the novel "Niels Lyhne by the Danish author I. P Jacobsen. The entropy determination is tabulated in Table 3

In Table 3 the letter H indicates entropy while the subscript indicates the number of symbols involved in the computation: e g., the heading H_3 indicates that the entropy values was computed from three consecutive symbols. In each of the three samples, it is seen that the entropy value decreases as the length of the word increases, illustrating the fact that the uncertainty of guessing the following letter and hence the entropy value, becomes less after the first five letters or so are known than if only one or two letters are known. This is also confirmed by the values for I P Jacobsen's work being greater at every level tabulated in Table 3 In the case of the speech samples, the description of the test picture given by the very intelligent 12 year-old boy includes three times as many symbols as the description by the 65-year-old woman, whose speech is much less informative (lower entropy).

Computer analysis of speech permits the

Table 3 *Entropy values for one written and two spoken language samples from three normal subjects*

Sample	Entropy values						Number of symbols in the sample
	H	H_0	H_1	H	H_2	H_4	
I P Jacobsen "Niels Lyhne	4 01	3.53	3.05	..61	2.23	1.93	4096
Boy 12 years QCA method	3 90	3 31	2.75	2 32	1 97	1 70	1847
Woman, 61 years QCA method	3 80	3 09	2.46	..01	1.68	1 45	641

examination of various parameters, e. g. the frequency with which various words occur This factor provides information of the information value of the sample as this value increases with the number of different words used This factor which was introduced by Johnson (1939) to characterize the value of a text is called the type token ratio or TTR The TTR is the ratio of the number of different words to the total number of words in the sample.

ANALYSIS OF LANGUAGE IN PATIENTS WITH DOWN'S SYNDROME

Speech

The electro-mechanically counted letters of the QCA method were supplemented by computer analysis of tests performed with mongoloids. In the case of spoken language a pair of twins were selected to illustrate the process The twins are 13 years old the boy is mongoloid while his sister is normal Both children have been brought up at home but as the family has travelled widely and lived in various countries throughout the world the children have experienced intense linguistic stimulation Owing to this experience combined with an otherwise stimulating family atmosphere on the whole the 13 year-old boy with Down's syndrome is significantly different from typical mongoloid subjects of the same age who have been institutionalized from early childhood

Table 4 *Description of the test picture given by a 13 year-old boy with Down's syndrome and by his normal twin sister analysed by electro-mechanical counting of letters*

Subject	Quick check analysis		
	Words min	Average Word length	Nouns (per cent)
Girl normal	145	3 91	24.5
Boy mongoloid	74	3 75	30.0

Table 5 *Computer analysis of the test-picture descriptions given by the 13 year-old boy with Down's syndrome and by his normal twin sister*

Subject	Entropy values		
	H_1	H_2	H_3
Girl normal	4 0	3.36	2.73
Boy mongoloid	3 97	3 45	2.58

The normal twin sister was taken as the norm for comparison in both methods of analysis This was necessary because no language analyses for English-language home-raised mongoloids was available To a certain extent, the normal twin sister's linguistic development must express the approximate level her brother would have reached if he had not been a mongoloid.

Both children were tested with the QCA picture at the same time The results are shown in Table 4

The figures listed in Table 4 indicate that the boy with Down's syndrome produced speech with a greater occurrence of nouns, and with words having fewer letters, than his normal twin sister Both relations suggest a less developed linguistic ability in the mongoloid

The entropy values for the normal girl and the boy with Down's syndrome (Table 5) do not differ sufficiently to permit their linguistic abilities to be differentiated by the use of entropy analysis

Comparison of the figures listed in Tables 4 and 5 indicate that computer analysis does not provide more information than was disclosed by the QCA analysis, which seemed to show that the mongoloid boy used a more primitive language than his normal twin sister

Computer Analysis of the Vocabularies

The vocabularies of the two children tabulated under the computer analysis may provide the

Table 6 *Results of computer analysis of the total vocabularies used by the two children during the test period The nouns which were not used by both of them are listed*

Normal Girl			Boy with Down's syndrome
Basket	Hair	Song	Cigar-holder
Bow	Mother	Spot	Flowers
Children	Overall	Table	Lot
Cloth	Paintbrush	Tulips	Man
Door	Picture	Vase	Jersey
Father	Pot	Weather	Shorts
Fence	Pull-over		Shirt
Fun			Woman
	Special nouns: 22		Special nouns: 9
		Nouns in common: 28	

basis of a semantic analysis of the text texts, but this is beyond the aims of the QCA analysis.

The nouns used exclusively by each of the two children in describing the test picture are tabulated in Table 6. It may be seen that the normal girl used differentiated words such as father mother and tulips, while her mongoloid brother made use of less differentiated collective terms such as man, woman, and flowers.

Conclusions

On the basis of experience with the use of quick check analysis in 250 normal persons of all ages, it was possible to use the quantitative speech analysis to characterize the speech of the boy with Down's syndrome as being the most primitive: he used relatively more nouns and words of shorter average length than did his normal twin sister. This analysis could be carried out without previous knowledge of the examined twins' data.

Computer analysis, which permits a semantic evaluation, confirmed that the above-mentioned results are correct. While the normal twin sister used specific terms, her brother with Down's syndrome made use of collective terms, which is an expression of the lower development of his linguistic abilities.

In this example, the measurement of entropy values, which can be done only by means of a computer analysis, did not support the results previously obtained by quick check analysis.

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TREATMENT OF DELAYED SPEECH DISORDERS

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The primary requirement in the treatment of delayed speech development is a thorough examination Frequently it is possible only during the course of treatment to discover the real abilities of these children Evaluation of this problem demands a large team who together—on the basis of examination—plans a suitable line of therapy for each child. The team determines the best type of school and as far as possible supervises continued therapy It is essential that the parents active co-operation is secured, since these children are likely to have difficulties later on at school If a child can be helped to get on successfully at school in the early stages, it may have a favourable effect on its entire future

The causes of delayed speech development have been studied since 1961 in the Audiophoniatric Section of the Department of Otolaryngology University of Helsinki We have also tried to develop the treatment of these children as far as available facilities have allowed

A team (Böhme, 1966) consisting of a large number of people co-operate in this rehabilitation work a phoniatrician, an audiologist a psychologist two speech therapists, a social nurse a kindergarten teacher two auditory rehabilitation assistants, a physiotherapist, ward nurses and children s nurses, as well as a primary school teacher The phoniatrician and the audiologist examine the patients and refer them to specialists in other branches of medicine This is necessary because they may suffer from multiple handicaps, often combined with minor brain lesions In addition to neurological examination and electro-encephalography there is a need for examinations by other specialists, e g. the otologist, ophthalmologist, child psychiatrist and paediatrician. Of this team those who are essentially in charge of the rehabilitation are the speech therapists, the psychologist, the kindergarten teacher and the physiotherapist, but the entire hospital staff is also involved in the work

The *psychologist's* responsibility is

I to *evaluate the child's abilities* by

a. standardized test methods, verbal and non-verbal and

b observation of the child both in individual play situations in a special therapy room and in group situations in the ward (Harding, 1965)

From these tests a picture is obtained of

1 the child s *intellectual ability*
—the present level of performance
—the capacity to develop

2. *emotional and social maturity*

3 *school maturity* a suitable type of school is recommended

II *Psychotherapy* for the children who show definite psychic abnormality resulting from delayed speech development. Psychis disturbances are very common when such an important medium of human communication as speech is defective

These children are usually either

1 timid and withdrawn or

2 restless and aggressive

III The psychologist s task is also to *explain to the parents the child's abilities and possibi-*

lities (Eraamie, 1964) and try to make them accept their child and take an interest in its rehabilitation. The psychologist should keep in touch with the local child-guidance clinic, with the teachers and with other persons in charge of continued rehabilitation.

The *speech therapist* is responsible for (Seeman, 1965):

I *The development of the child's language communication*

1 Establishment of a good contact between the child and the speech therapist.
2. Improvement of language ability by means of play therapy:
a. improving the power of concentration,
b. motivation and stimulation of the child to use voice and speech,
c. development of "inner language" (thought) and rousing of symbol function (Myklebust, 1957),
d. widening of passive vocabulary using at first different objects, toys and games,
e. familiarizing the child with the world of sound by means of various sound sources,
f. training the child's auditory discrimination and auditive memory
g. stimulation and widening of active vocabulary
h. training the motor activity of the speech organs.

Initially the instructional materials include only objects, various toys, etc. (Wood, 1964). Later pictures and drawings are added, which are already more abstract. The therapy aims at getting the child to express itself spontaneously which goal is most easily attained by means of play and games (Berry & Eisenson, 1956).

The rehabilitation of these children is individual, and treatment demands much experience on the part of the speech therapist. She should take the child's entire personality into account and not confine herself to the language problem alone.

II *Speech instruction proper*

This can only be started when the child has acquired enough language to make self-expression of some kind possible:

1 Continual widening of the vocabulary
2. Correction of articulation:
   a. word patterns,
   b. sounds (vowels, consonants and their combinations)
3 Correction of sentence structure, grammatical errors.
4 Correction of reading and writing disturbances.
5 Exercises in the use of the voice.
6 Correction of rhinophonia.

III *Guidance of parents*

The speech therapist should advise the parents as to how to handle their child and what to do at home to promote language ability

The role of the kindergarten teacher in rehabilitation

I. *Improvement of* the child's *auditive abilities* using various *singing games* with easy words, *rhythmic exercises* and development of the child's *musical* ability (various instruments)

II *Visual-motor exercises*

handicrafts, jigsaw puzzles, modelling, drawing, painting, etc.

III. Accustoming the *child to group activities*

Daily exercise of this kind, lasting 3 hours, seems to develop the children considerably. Although all children cannot be made to participate in games, they do at least look at the activities of the others, and may perhaps join in another time.

In the case of children whose movements are awkward and poorly developed, daily rehabilitation includes physiotherapy given by a qualified physiotherapist.

The older children—including the 6-year-olds—attend elementary school lessons daily where

they are taught by a primary school teacher This brings to light the child s attitude towards schooling.—The older boys also receive training in wood work twice weekly

In addition to individual therapy teaching in groups can be used if suitable groups can be formed

The team meets twice weekly to discuss the results. An attempt is made to sum up the child s abilities, qualities and capacity to develop and on this basis, to find a suitable type of school and organize continued therapy either in kindergartens or by speech teachers, etc

The acquisition of language involves a process of learning which may often require years of therapy (Van Riper 1961 1965) The best results are achieved if the parents participate actively in the rehabilitation They should accept their child as it is and encourage it to express itself It should be remembered that these children have difficulties at school If they are helped with their school work from the start, in parallel with continued rehabilitation, then these difficulties can be overcome. The child should learn to read and write during the first two school years. If they are *poorly grounded they will not like attending* school, and their achievements there will be poor This will later affect them in their occupation and in their whole life

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DISCUSSION

I Leegaard Do all these children have hearing defects, or are there other reasons for their retarded speech, i e brain or mental defects? If so is the programme for rehabilitation the same in all groups?

B Fritzell What was the lower age limit for starting therapy? What was the average duration of therapy during which the children were institutionalized in the phoniatric ward?

S Siirala (Reply to Leegaard) Causes of the delayed speech were

		No. of cases	Per cent
I	Central disorders of *language development*	113	33 7
II	Speech disorders resulting from hearing loss	101	30.1
III	Pathological changes in the speech organs	33	9 9
IV	Mental retardation	49	14 6
V	Stuttering	10	3 0
VI	Psychoneurotic disorders of speaking	29	8.7

The type of brain damage is very complicated in these cases.

(Reply to Fritzell) Most of the patients come for treatment at the age of 6 years. Treatment may also start earlier

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A RESEARCH PROGRAMME ON STUTTERING AND STRESS

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A series of experimental stressor exposures is described, in which groups of stutterers had to expose their speech disturbance in public. The subjects' self-rated emotional reactions are compared with their sympatho-adreno-medullary "stress" reactions, as reflected by urinary excretion of catecholamines. The effect of iteration of the experimental situation and the influence of psychotrophic drugs were also studied.

In the autumn of 1965 a programme for research on stuttering was initiated on a co-operative basis between the Laboratory for Clinical Stress Research and the Department of Phoniatrics at Karolinska Sjukhuset, Stockholm. Certain aspects of the planning and the methods in one of the investigations were presented at the Helsinki Congress in 1966 (Leanderson and Levi, 1967). Here we wish to survey and briefly report on the background to the research programme and the studies carried out so far. The latest study was conducted in the middle of June this year.

A review of the literature on stuttering reveals an inconsistent and somewhat obscure picture of the causes and development of the syndrome. This is partly due to the complex nature of the problem, but also to the incompleteness of the data on which the authors base their opinions. Most investigators agree, however, that the attitudes of the social environment are of great significance, at least in the development of the syndrome. Clinical experience also indicates that the stutterer attaches great importance to the listener's reaction to his speech. His self criticism and strong ambition to speak without stuttering often cloud his experience of the listener's reaction.

I Exposure to Televised Stuttering

How then do non-stutterers react to stuttering, and how do stutterers react, when faced with the same situation? To study this question under controlled conditions we prepared television recordings of a standardized interview with severely stuttering patients and then played back these interviews to an audience consisting of the subjects in the experiment. By using such recordings one avoids an interaction between stutterer and audience and thereby keeps the stimulus situation under control. The present audience comprised three groups, each with five subjects, two of the groups being made up of stutterers. One of the latter groups comprised active members of a society of stutterers in Stockholm, who thus had experience of regular contact with stuttering, while the other group lacked such experience. The third group consisted of non-stuttering controls. The showing of the televised interviews took two hours and was preceded and followed by a control period of two hours. Biochemical variables, including urinary excretion of adrenaline, were measured (Euler and Lishajko 1961) and the subjects rated their subjective reactions, such as "unpleasantness" on an 11-point scale.

The adrenaline excretion in the three groups is shown in Fig. 1 with the adrenaline output plotted against the vertical axis. The non-

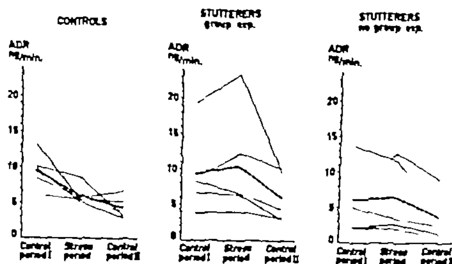


Fig. 1 Urinary adrenaline excretion in controls (left), stutterers with group experience (middle) and stutterers without group experience (right) during control conditions and during viewing and listening to televised interviews with severely stuttering patients. *Broken lines indicate mean values.*

stutterers—left figure—showed a small range and a *decreasing* tendency throughout in agreement with the circadian rhythm in adrenaline excretion (Leanderson and Levi 1966) The two groups of stutterers, on the other hand, showed great interindividual differences, with *an increasing tendency in mean adrenaline* excretion during the television period

Fig. 2 shows the subjects ratings of their experiences in the variable "general emotional arousal" It may be seen that all three groups reacted similarly The group of non-stutterers, however included two persons who reported indifference.

Thus, the stutterers exhibited a stronger adrenaline reaction than the non-stutterers, but did not report stronger emotional reactions. *This may be due to psychological defence* mechanisms possibly present in the stutterers, e g denial.

2 *Reactions to Psychotropic Drugs under Basal Conditions*

To study the reactions of stutterers to psychotrophic drugs, *an explorative study* was undertaken under controlled basal conditions. Strict instructions were given about sleep, smoking, intake of food and fluid, etc. during the last 24 hours before the evening of the investigation (cf Levi, 1967) The experiment comprised three two-hour periods—control period, *drug period, and post-drug period.* Urine samples were collected at the end of each period and *emotional experiences* were self rated every half hour The 49 subjects had been *randomly grouped.*

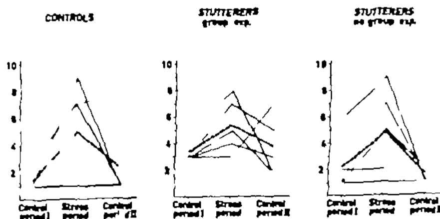


Fig. 2. *Self-rated general emotional arousal during the conditions* and in the groups described in Fig. 1 (1 point = no arousal, 11 points = extreme arousal).

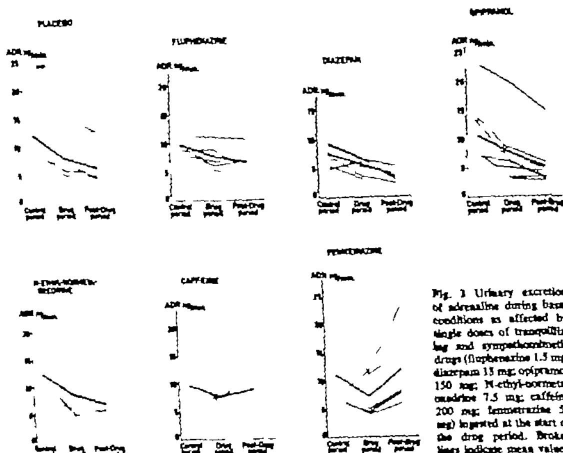


Fig. 3 Urinary excretion of adrenaline during basal conditions as affected by single doses of tranquillizing and sympathomimetic drugs (fluphenazine 1.5 mg; diazepam 15 mg; opipramol 150 mg; N-ethyl-normetanephrine 7.5 mg; caffeine 200 mg; fenmetrazine 50 mg) ingested at the start of the drug period. Broken lines indicate mean values.

Fig. 3 shows the adrenaline excretion of the subjects after single doses of three tranquillizers and three sympathomimetics, respectively and a placebo all administered at the start of the "drug period". The reactions in the placebo and tranquillizer groups reflect the decline in adrenaline excretion due to circadian rhythm, whereas the groups given sympathomimetics exhibit an increasing trend during the post-drug period. Self-rated "stress" was low in all groups and during all periods. No significant drug effects could be demonstrated, probably because the subjects were under basal conditions throughout the experiment.

The results during these basal conditions are similar to those one would expect from a normal population. The study also provided information concerning base-line levels of the stutterers for the experimental situation that was to be used in subsequent studies.

3 *Reactions to Public Speaking in Stutterers and Non-stutterers*

The next step was to let 14 stutterers expose their speech disturbance in a standardized experimental situation. This now lasted four hours, a control period of two hours being followed by a two-hour speech period. During the speech period, the subjects were asked several times and in random order to read a text and to describe pictures projected onto a screen. On a later occasion, 15 non-stutterers (former hoarseness patients) were exposed to the same situation, serving as controls.

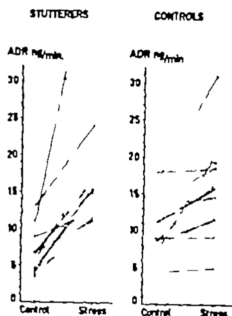


Fig. 4 Urinary excretion of adrenaline before and during a stressful situation (public speaking) in stutterers (left) and in non-stuttering controls (right). Broken lines indicate mean levels.

Figure 4 shows the adrenaline excretion in stutterers and non-stutterers in the control and the speech periods It may be seen that the increase amounted to 150 per cent for the stutterers but only to 40 per cent for the controls This strong reaction in the stutterers—some values were among the highest ever recorded in the stress laboratory—are reflected by the self ratings (Fig. 5) The curves show that the stutterers reported an increase in unpleasant feelings during the speech period and

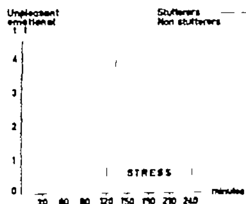


Fig. 5 Mean self ratings of "unpleasantness" in stutterers and non-stutterers during the conditions described in Fig. 4 (11 point scale).

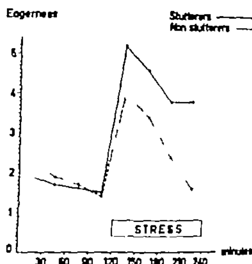


Fig. 6 Mean self-rated eagerness during the conditions described in Fig. 4

that the non-stutterers did not. However it may be noted that although many of the stutterers were observed as being clearly embarrassed and greatly inconvenienced, the emotional reactions reported by the stutterers were of a moderate intensity

As regards self ratings of experienced "eagerness" (Fig. 6) the reaction was fairly similar in the two groups though the stutterers reported

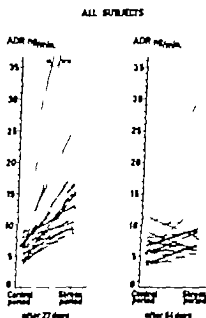


Fig. 7 Urinary adrenaline excretion in a group of stutterers before and during public speaking following drug treatment for 27 days (first session, left) and 54 days (second session, right). Broken lines indicate mean values.

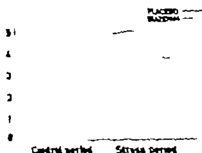


Fig. 8. Pooled mean self-ratings of "stuttering tendency" before and during public speaking in 20 stutterers after short-term treatment with placebo and diazepam (11-point scale).

somewhat higher values. A possible, tentative speculation concerning the relationships between the physiological and psychological reactions is that a positive experience, such as "eagerness" would be paralleled by a moderate increase of adrenaline excretion, whereas a negative experience, such as "unpleasantness" could be paralleled by a more marked increase.

4 Drug and Habituation Effect on Stress Responses during public Speaking

The study of reactions in stutterers to public speaking was also designed to include effects of long-term medication and of "habituation". Opipramol (50 mg × 3), diazepam (5 mg × 3) and placebo were administered in a double-blind cross-over design during two consecutive periods of 27 days each. The stutterers were exposed to the public speech situation twice, namely at the end of each period of medication. The catecholamine excretion levels as well as the psychological self-ratings exhibited marked "habituation" effects, i.e. the reactions were less pronounced during the second exposure.

Thus, it will be seen from Fig. 7 that in several subjects the adrenaline excretion this time actually decreased from the control to the speech period. This was reflected in a corresponding decrease in the emotional reactions reported by the subjects.

As concerns drug effects, we found that opipramol did not modify the stressor induced adrenaline increases during any of the exposures. On the other hand, 54 days of diazepam treatment were accompanied by a turn of the stressor-induced adrenaline increase into a decrease. Although this group comprised only two subjects—three of the original five dropped out during the course of treatment—these data justified a further study on the effects of long-term diazepam treatment.

5 Effects of Short and Long-Term Treatment with Diazepam

Two separate diazepam trials have been made, one with a single day of treatment (5 mg × 3), to study the effects of short-term medication, and one with this dose for 54 days. The subjects of these two trials were taken from the waiting-list for stuttering therapy.

In the one-day treatment trial, using the double-blind cross-over design, diazepam (n = 14) and placebo (n = 15) were administered on two days at an interval of one week. The data are still being processed, but preliminary results indicate a drug effect in the following respects.

The self-ratings of "stuttering tendency" while the subjects were on diazepam and placebo, respectively, are shown in Fig. 8 (pooled ratings from both occasions, n = 20). It will be seen that throughout both periods the stuttering tendency was rated lower if the subjects were on diazepam.

Figure 9 shows the self-ratings of "stress"

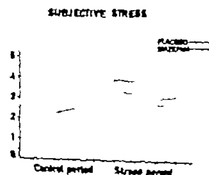


Fig. 9. Pooled mean self-ratings of "emotional stress" in the subjects during the conditions indicated in Fig. 8.

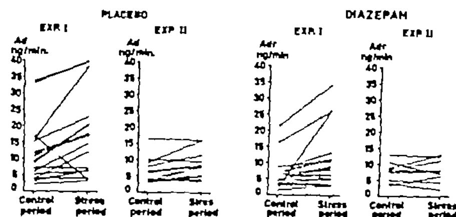


Fig. 10. Urinary adrenaline excretion after one day of placebo treatment (left) and diazepam treatment (right). Experiment 2 was conducted one week after Experiment 1 Broken lines indicate mean levels.

during the same trial A similar drug effect was noted here.

It may be seen from Fig. 10 that the adrenaline excretion levels during the first session were lower in the diazepam group

In the 54-day treatment trial, the adrenaline excretion of the diazepam (n = 11) and placebo (n = 5) groups is shown in Fig. 11 The mean increase in the placebo group was about 200 per cent In the diazepam group the rise was more moderate in several subjects the excretion remained on a low level throughout the session.

Other data from this study—derived from the diaries kept by the subjects, ratings during the experimental sessions, personality inventories, and the patients histories as regards stuttering—have still to be analysed. Further reports on these studies will be published.

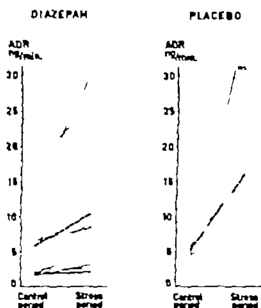


Fig. 11 Urinary adrenaline excretion in stutterers after 54 days of diazepam (left) and placebo (right) before and during public speaking. Broken lines indicate mean levels.

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THE SITUATION OF THE LARYNGECTOMIZED PATIENT

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The patients' psychological and social problems in connection with laryngectomy have been studied by an extensive pre- and postoperative inquiry. Smoking habits seemed to decrease postoperatively, whereas no influence or a slight increase in the consumption of alcohol was registered. Some patients experienced depression, more often as a reaction to the impairment of speech rather than to the diagnosis of cancer. Most of the patients under 65 have learnt to communicate by oesophageal speech and are also working full-time in their original occupations. The importance of careful pre-operative penetration of surgical, mental and socio-medical problems as well as oesophageal speech demonstrations is emphasized. This is best achieved by intensive information given to the patient, his relatives and his employer by a team consisting of the surgeon, the phoniatrist, the logoped and the social worker.

The incidence of laryngeal cancer has increased in Sweden as well as in many other countries during the last decade. The reason is not known. Smoking has been supposed to be an important aetiological factor and the increasing industrial outlet of dusts and fumes has also been suspected. In the opinion of most authors, stage I of laryngeal cancer can be successfully treated by radiotherapy. Stages II and III also seem to have a fairly good prognosis, provided prompt and adequate surgery is performed. In spite of this, however, it is clear that great social problems will appear for the individual patient after the operation. The loss of normal voice constitutes indeed a great handicap, but not to such an extent that necessary and well planned surgical intervention needs to be postponed in favour of radiotherapy alone. The aim of this report is to present a pilot study regarding medical, social and psychological problems in connexion with laryngectomy in order to obtain information of the patients' reactions and the degree of handicap after this type of operation.

METHOD AND MATERIAL

The patients were checked from three points of view from the moment of diagnosis through the pre- and postoperative stages and also during a rehabilitation period of varying length. The follow-up programme included repeated personal interviews, which were completed by an extensive questionnaire containing 100 questions. This had been prepared in collaboration with sociologists and psychologists.

This preliminary report includes only 27 cases. A more extensive survey including a brief review of the relevant literature is in preparation (Kitzing & Toremalm, 1970). Only problems regarding speech rehabilitation, occupational rehabilitation, smoking habits, alcohol consumption and some psychological reactions after the operation will therefore be summarized here.

The number of patients, who were all men, and their ages at operation are shown in Fig. 1. Seventeen patients were under 62 years, while 10 were over 65. Eight patients had from the beginning been judged appropriate for radiotherapy in spite of a growth which was classified as at least stage II. They were, however, later subjected to operation owing to recurrence of their cancer or insufficiency of pre-

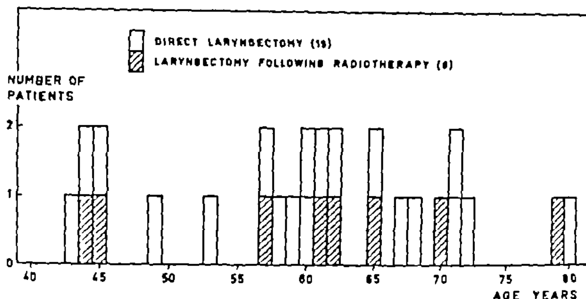


Fig. 1 Distribution of the patients according to age and pre-operative treatment

liminary treatment Neck dissection was indicated only in three cases without obvious influence on their ability to practise oesophageal speech

RESULTS AND DISCUSSION

It is always difficult to make an objective estimation of the effectiveness of oesophageal speech ability We have in our study practised a type of double control The patients subjectively estimated their own capacity to speak comfortably and to make themselves understood in different social situations. This control was supplemented by repeated tape recordings and by the logoped's opinion. In this way a satisfactory evaluation was possible. The results are shown in Fig. 2. It is clear that the age of the patient is of great importance in speech rehabilitation Among eight patients over 67 only one attained good verbal ability Below 65 however speech rehabilitation was nearly 100 per cent. Only two men in this group failed to learn to speak One of them had been treated for schizophrenia for many years and the second was an uncommunicative independent workman Three patients, of

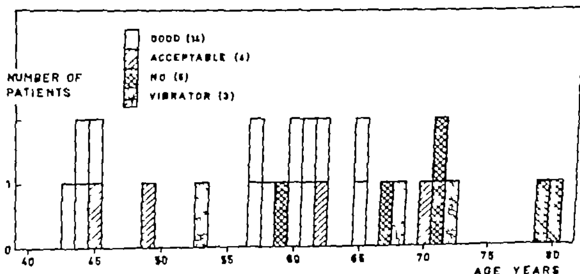


Fig. 2. The patients ability or failure to learn oesopl

ter long but fruitless training, had to be equipped with an "artificial larynx" (vibrator). Thus, a total of 18 patients became good oesophageal speakers (67 per cent). This agrees with previous reports on series of unselected patients from Europe and the U.S.A. (Horn, 1962 Seeman, 1958)

Many questions were designed in order to observe psychological reactions to the operation. The investigation confirms an earlier supposition, viz. that patients with cancer of the larynx very often are compulsive smokers and heavy drinkers (Nahum & Golden, 1963). It is, however not possible to decide if these statements have had an aetiological influence because these questions are of a very complex nature Another aetiological factor which does not seem to be given sufficient attention in the literature, is the effect of chemical air pollution. As many as 19 of our patients had been exposed to air contamination during long periods, either in their present or a previous occupation. Above all, metal dusts and chemical fumes were reported

The patients smoking habits are illustrated in Fig. 3 Before the operation, there were two non-smokers and 19 heavy smokers with a consumption exceeding 20 cigarettes a day The patients had, on the average started to smoke when they were between 14 and 17 years of age Postoperatively most patients stopped smoking and none smoked heavily Five patients are still moderate smokers. Instead of smoking through the tracheal stoma, they have learnt to practise a special mouth-puffing technique which may not be dangerous with regard to a concomitant bronchial cancer

Contrary to smoking habits, alcohol consumption does not seem to be influenced statistically by the operation (Fig. 4), but it must be borne in mind that subjective information as to drinking habits must always be looked upon with scepticism. Our findings based on frequent postoperative consultations and our good contact with the patients relatives suggest that a moderate increase in alcohol consumption occurs postoperatively This is also in accordance with previous French and American reports (Valley & Cornut, 1962 Webb & Irving, 1964) The increased alcohol consumption may be a symptom of some depressive neurosis, which can prevent effective speech training and thus delay the patient's rehabilitation.

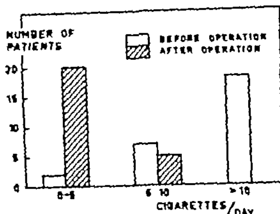


Fig. 3 Pre- and postoperative smoking habits.

Only 10 of our 27 patients had gone through the operation without any signs of depressive reactions. Among those who suffered from such symptoms, only five could be classed as severe cases, but none of them had contemplated suicide. Depression was most pronounced in the period between diagnosis and operation. It seems therefore valuable to keep the patients with laryngeal cancer under close observation and give them adequate and frequent information during this period. We have prac

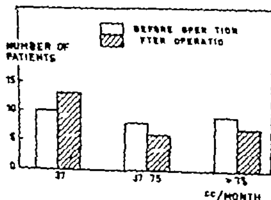


Fig. 4 Information as to alcohol consumption given by the patients.

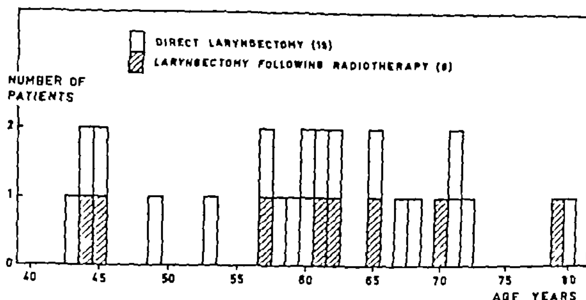


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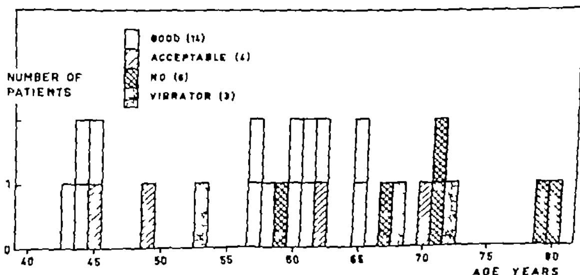


Fig. 2 The patients ability or failure to learn oesophageal speech.

opinion that psychological considerations are as important as medical and surgical ones, and that they are often overlooked or underestimated for the sake of purely technical problems.

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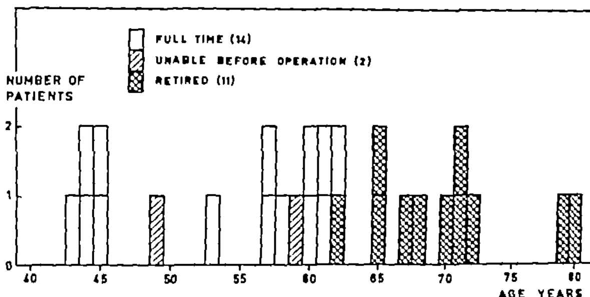


Fig 5 Age distribution working capacity and occupational rehabilitation

tised group information given by the surgeon, the phoniatrist, the logoped, the social worker and, last but not least confronted the patient with a well rehabilitated and good oesophageal speaker

Many authors report a period of depression in direct connexion with the operation due to the enforced postoperative aphonia. Such reactions were seen in only two of our patients. We believe that this shows that the pre-operative information was not only sufficient but also exerted a positive influence on the course of healing The greatest psychological problem was obviously the loss of the normal voice This was stated by 13 patients before the operation and none of them had changed opinion 6 months later The fear of cancer *per se* was initially indicated as the most serious problem by 12 patients. This figure was, however reduced to nine immediately after the operation and to only seven 6 months later Thus, the fear of cancer decreases as a result of a post operative course without complications.

Only five patients were worried about their occupational situation and the family economy after the operation. The best help to overcome these problems was provided by close relatives in 15 patients and by the above mentioned team of informers in 13 Seventeen patients reported postoperatively the same good mental condition as they had had before the operation whereas seven had become more restless and nervous

It is a well known fact that some deaf persons often have a tendency to be aggressive due to difficulties in establishing personal contacts. We found the same reaction in three cases after laryngectomy followed by insufficient speech rehabilitation, and presume an analogous explanation for this. Fortunately enough, 22 patients expressed the opinion that relatives, friends, and also strangers, are appreciative of their strange handicap The same patients also stated that the thorough information, the listening to a good oesophageal voice and our preliminary contact with the respective employers had been the most positive steps to prevent depressive reactions

Finally some information as to occupational rehabilitation will be of interest. Most patients under 65 years returned to their former work, and only a few changed occupations (Fig. 5). The only exceptions were again the schizophrenic mental patient and a chronic alcoholic addict.

Although the present case material is small, it has given us a good insight into the patients reaction patterns. The extensive questionnaire and the repeated interviews may be considered overambitious as a routine but we are of the

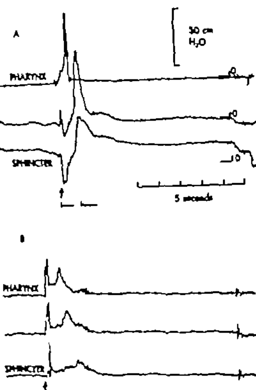


Fig 1

RESULTS AND COMMENTS

Measurements were performed on 20 patients, most of them were studied before and at certain intervals repeatedly after laryngectomy In most cases, healing occurred without complications, and none of the patients complained of dysphagia, although pre-operative radiotherapy had been given to several of them. In one patient who had received pre-operative radiotherapy for a supraglottic cancer a hypopharyngeal fistula developed. However this healed rapidly after which the patient acquired a good oesophageal voice.

The recordings from three typical cases are presented here.

Fig. 1 shows deglutition pressures from a 59-year-old man given pre-operative radiotherapy before laryngectomy The pressure recordings were made simultaneously from a segment of a length of cm from the pharynx to the sphincter The arrows mark the onset of deglutition after administration of a sip of water Before operation (A) the elevated resting pressure in the sphincter is decreased and the pressure in the pharynx is increased by swallowing, as is normally found. During swallowing, the pressure in the sphincter rapidly increases and returns to normal resting tonus. The increased pressure passes into the oesophagus, in which a wave of peristalsis starts. The recordings show normal pre-operative function of the pharynx, hypopharynx and oesophageal sphincter Postoperatively (B) the elevated resting pressure in the sphincter is not detectable, and swallowing a sip of water (arrow) causes no decreased pressure in the sphincter The pressures in the pharynx and sphincter increase simultaneously and rather weakly After the first few contractions, another weak wave of contraction initiates without complete relaxation, indicating a tendency to slight spasm in the scarred region of the hypopharynx. Similar pathological pressure recordings were found in all but one of the patients after laryngectomy Only one patient complained of dysphagia. He was 80 years old and revealed a heavy spasm in the sphincter postoperatively and did not acquire an oesophageal voice.

Fig. 2 shows the curves from a 49-year-old man with recurrent laryngeal cancer which had been treated by radiotherapy 2 years before. The patient was hoarse, but he had no dysphagia. The curves in A were recorded before laryngectomy when the patient belched voluntarily During an oesophageal ructus, the upper part of oesophagus is relaxed by voluntary muscles, which brings about a negative pressure. The two arrows indicate the aspiration of air during inspiration. The recordings were made from a 10 cm segment of the body of the oesophagus and show that the negative pressure phase is followed by the ructus: An increased pressure is recorded in the oesophagus, and the air is momentarily pressed upwards without any antiperistalsis. Swallowing of a sip of water (arrow) results in a normal wave of peristalsis. The curves in B show the condition 1 month after laryngectomy when

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MOTILITY OF THE PHARYNX AND OESOPHAGUS AFTER LARYNGECTOMY

N Sandberg

From the Department of Otolaryngology University of Göteborg Sahlgren's Hospital Göteborg Sweden

Intraluminal pressure recordings were made from the pharynx and the oesophagus in patients with laryngeal cancer Before the laryngectomy no pathological recordings were found After the operation none of the patients complained of dysphagia, but most of them showed well-defined alterations in the intraluminal pressures. After swallowing, relaxation and contraction pressures and resting tonus in the pharyngo-oesophageal sphincter were weaker Peristalsis in oesophagus was usually good The importance of early training of the oesophageal voice is stressed. Early function of the hypopharyngeal wound area seems to be important.

Laryngectomy disturbs the co-ordination of deglutition respiration and voice normally performed by the larynx. The vocal powers are lost and a permanent tracheostomy is made Despite derangement of "the nutritional way" caused by laryngectomy the function of the pharynx and oesophagus after laryngectomy seems to be surprisingly good, and dysphagia is no common symptom after the early post operative phase Usually the patients are soon able to take adequate amounts of food. The important practising of the oesophageal voice can also be started early which seems to be of importance in order to obtain a good result

Normal and abnormal deglutition with special reference to partial laryngectomy was studied by Ogura and his coworkers (Ogura *et al* 1964 Ogura & Mallen, 1965 Staple & Ogura, 1966) The aim of the present investigation was to study the motor function of the pharynx, hypopharynx and oesophagus after laryngectomy by measurements of intraluminal pressures, since very little is known of what happens to the act of swallowing after the operation. The patients were examined before and after laryngectomy by electro-manometrical recordings from the pharynx, from the pharyngo-oesophageal sphincter and from the body of the oesophagus. The muscles which are of principal interest in the region for the study are the inferior constrictor and the crico-pharyngeal muscles innervated by a branch of the vagus through the pharyngeal plexus (Lund & Ardran 1964)

METHODS

The motor activity was examined by measurements of intraluminal pressures in the pharynx and oesophagus and in their junction, mainly according to the principles of Code *et al* (1958). A system of water filled open-tip polyethylene tubes were introduced through the nose and adjusted to the desired positions. The nasal ends of the tubes were connected to electromanometers, and pressures were recorded on a direct writing 8-channel ECG apparatus (Mingograf Elema-Schönander AB Stockholm, Sweden) from *three* different levels simultaneously The three tips were positioned at a distance of 1 or 5 cm from each other thus allowing recordings from segments of 2 or 10 cm The resting pressures, the deglutition pressures after swallowing a sip of water and the oesophageal ructus pressures were recorded.

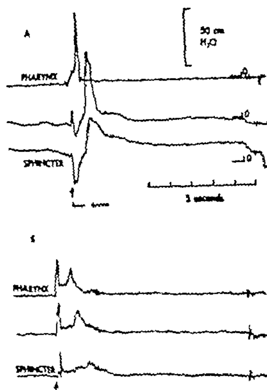


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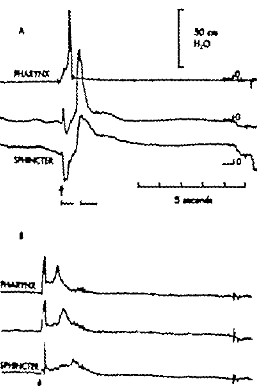


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Measurements were performed on 20 patients, most of them were studied before and at certain intervals repeatedly after laryngectomy. In most cases, healing occurred without complications, and none of the patients complained of dysphagia, although pre-operative radiotherapy had been given to several of them. In one patient who had received pre-operative radiotherapy for a supraglottic cancer a hypopharyngeal fistula developed. However, this healed rapidly after which the patient acquired a good oesophageal voice.

The recordings from three typical cases are presented here.

Fig. 1 shows deglutition pressures from a 59-year-old man given pre-operative radiotherapy before laryngectomy. The pressure recordings were made simultaneously from a segment of a length of 2 cm from the pharynx to the sphincter. The arrows mark the onset of deglutition after administration of a sip of water. Before operation (A) the elevated resting pressure in the sphincter is decreased and the pressure in the pharynx is increased by swallowing, as is normally found. During swallowing, the pressure in the sphincter rapidly increases and returns to normal resting tonus. The increased pressure passes into the oesophagus, in which a wave of peristalsis starts. The recordings show normal pre-operative function of the pharynx, hypopharynx and oesophageal sphincter. Postoperatively (B) the elevated resting pressure in the sphincter is not detectable and swallowing a sip of water (arrow) causes no decreased pressure in the sphincter. The pressures in the pharynx and sphincter increase simultaneously and rather weakly. After the first few contractions, another weak wave of contraction initiates without complete relaxation, indicating a tendency to slight spasm in the scarred region of the hypopharynx. Similar pathological pressure recordings were found in all but one of the patients after laryngectomy. Only one patient complained of dysphagia. He was 80 years old and revealed a heavy spasm in the sphincter postoperatively and did not acquire an oesophageal voice.

Fig. 2 shows the curves from a 49-year-old man with recurrent laryngeal cancer which had been treated by radiotherapy 2 years before. The patient was hoarse, but he had no dysphagia. The curves in A were recorded before laryngectomy when the patient belched voluntarily. During an oesophageal ructus, the upper part of oesophagus is relaxed by voluntary muscles, which brings about a negative pressure. The two arrows indicate the aspiration of air during inspiration. The recordings were made from a 10 cm segment of the body of the oesophagus and show that the negative pressure phase is followed by the ructus: An increased pressure is recorded in the oesophagus, and the air is momentarily pressed upwards without any antiperistalsis. Swallowing of a sip of water (arrow) results in a normal wave of peristalsis. The curves in B show the condition 1 month after laryngectomy when

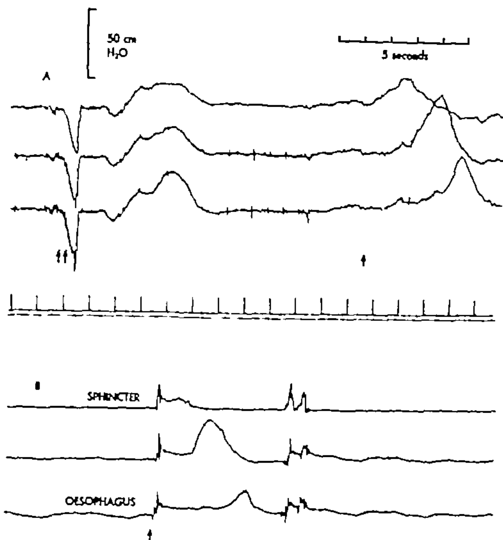


Fig. –

the patient had a good oesophageal voice Dry swallowing (arrow) results in a moderate contraction No resting tonus or relaxation phase is seen The contraction of the sphincter is followed by a wave of contraction in the oesophagus. Cineradiography showed moderate dilatation of the hypopharynx (Malmquist & Sandberg unpublished)

Fig 3 shows the deglutition curves from a 50-year-old man with very good oesophageal voice 5 years after laryngectomy and unilateral neck dissection. He had no dysphagia. During deglutition (indicated by arrow) a normal wave of contraction is recorded from the pharynx and hypopharynx. In the sphincter no resting tonus is seen only a tendency to relaxation followed by a weak contraction. When the patient says "Ja" with his oesophageal voice (two arrows) a moderately increased pressure in the hypopharynx and sphincter is seen. This contraction is followed by another showing pressure waves of the types seen during deglutition which is usually initiated after oesophageal ructus. The patient in Fig. 2 used the "aspiration method" to get an oesophageal voice the patient in Fig. 3 used the compression method

In most cases a good peristalsis was recorded from the oesophagus. After swallowing a sip of water two patients showed only weak segmental simultaneous contractions, i e showed signs of hypomotility This was seen in one very old patient and in one with recurrent laryngeal cancer treated with radiotherapy one



Fig. 3

year before. These two patients did not acquire oesophageal voices, which most of the other patients managed.

DISCUSSION AND CONCLUSIONS

The investigation confirmed the assumption that dysphagia is not common after laryngectomy. Healing without complications occurred in all cases but one (hypopharyngeal fistula). The undisturbed act of swallowing could partly be explained by the elimination of the respiratory air from the pharynx. This simplifies swallowing, and no dysphagia is experienced despite well-defined alterations revealed by recordings of the intraluminal pressures. A moderate weakening of the striated muscles in the pharynx and the upper oesophagus resulting in low resting pressure in the sphincter and low power of relaxation and contraction would seem to be of minor importance. On the other hand it seems to be important that no spasm of the inferior constrictor muscle and cricopharyngeal muscle exists. This disturbs both swallowing and practising of oesophageal ructus. The 80-year-old man illustrated this. Staple & Ogura (1966) made the same observation after partial laryngectomy in studies with cineradiography.

It might be concluded that, as a rule, the disturbances of the swallowing mechanism recorded after laryngectomy seem to be of minor importance in the patients' nutrition, but they could explain why some patients cannot acquire an oesophageal voice despite good psychological condition postoperatively. Thanks to healing without complications the patients were able to start training their oesophageal voice early, as a rule 10 to 15 days postoperatively. For psychological reasons, it is important to start this training as early as possible, but it may also contribute to a good restitution of swallowing. Early training exposes the wound area to function (tension and strain) at a time when function improves the appropriate differentiation of the newly formed healing tissue. The importance of function for the maturation of the tissue in healing wounds has previously been stressed by Sandberg (1963).

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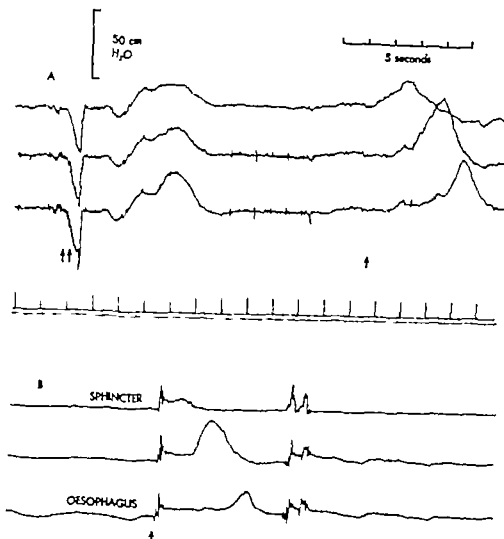


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apy and the patient thus had voice training for half an hour daily for 5 days a week. The numbers of treatments were: one patient had 16, the majority i.e. 13 patients, had 22–31 and one patient 41 including 13 after the end of radiation therapy

The treatment was started with slackening and relaxation of the recumbent patient followed by breathing exercises in order to teach the patient the subjective control of the air stream necessary for phonation and, after a while, phonation exercises by the method of Svend Smith with certain modifications. This type of voice exercises differs from others in that it makes use of a considerable supply of air among other things, in order to obtain the Bernoulli effect. In this way you get, a cautious but effective massage of the vocal cords. In the exercises the patient phonates primitive unarticulated sounds completely without linguistic connection, and they are delivered in tones of low frequency in sound series of unequal length and with a varying rhythm. The total time of treatment does not allow advanced exercises so the patient is only generally taught to use the vocal cords as well as circumstances permit, and as much as possible the ability of adaptation to changed conditions in the larynx.

Thus, in principle the radiological and phoniatric treatments are terminated at the same time, and most of the patients are then completely or almost aphonic. The number of days of treatment was about 25 which is to be considered low even for the treatment of a simple phonastenia, and it was not influenced by the premorbid voice quality of the patient, which naturally differed from person to person. Voice recordings were made after the end of the treatment and at all check ups. At the first check-up about 4 weeks later most of the patients had had a useful voice for about one week and at that time the mobility of the irradiated vocal cord as seen in stroboscopic light indicated absence of infiltrative processes in all patients. The patients also returned for check ups at 6 months and up to two years later. At these visits, the patients were also informed of the increased vulnerability in the treated tissues. When necessary some drug for the relief of coughing was prescribed.

RESULTS

In one patient out of the 15 the vocal cords atrophied so markedly that the cords could not be adducted closely enough to admit phonation, and about 18 months after the therapy he had to start phonating with the false vocal cords. Three of the other patients had slight oedema of the upper part of the vocal cords, which did not essentially reduce the phonatory mobility of the vocal cords, while the remaining patients had practically normal vocal cords. In this last group was a patient with relatively thick ventricular folds and with relatively severe phonastenic symptoms. All patients except the one with ventricular phonation had voice qualities well within normal limits. The great majority of the patients found voice treatment comfortable while it lasted, and declared that it was of good use also later on. According to some patients, their voices were better at the last check-up than before they fell ill. Some patients, including all with oedema, said that their voices had become deeper and darker than they were at first.

CONCLUSIONS

It is not possible to draw far-reaching conclusions from the series considered in this preliminary report, but it supports rather than contradicts the assumption that it is possible to decrease the risk of radiation damage by using phoniatric treatment, which is therefore recommended.

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PHONIATRIC TREATMENT COMBINED WITH RADIOTHERAPY OF LARYNGEAL CANCER FOR THE AVOIDANCE OF RADIATION DAMAGE

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From the Department of Otolaryngology University Hospital Lund Sweden

Patients with cancer of the vocal cords, which is treated by radiation therapy usually suffer considerable discomfort including deterioration of the voice during and for a varying period of time after the therapy In an attempt to keep the vocal cords otherwise healthy by reducing the fairly great risk of vocal abuse and secondary weakness of the cords, phoniatric treatment and radiation therapy are given in parallel It is suggested that this might be tried as a prophylactic measure against radiation damage to the vocal cords.

Radiation therapy is often given separately to two or more fields in order to spare healthy tissues as much as possible, but nevertheless the skin through which the rays pass becomes red and painful This reaction is often treated locally with some ointment. Gradually the field is browned and the patients are told that they should avoid exposing the field to strong sunlight

These precautions are also taken in radiotherapy of laryngeal cancer in order to spare the skin, but obviously it is not possible to protect the healthy tissues on which the radiation is concentrated i e. the closest vicinity of the tumour As is also generally known a large number of these patients sustain radiation injuries either in the form of atrophy of the tissues of the vocal cords or more commonly oedema of the vocal cords and/or in the arythenoid regions. This oedema usually persists for a long time and gradually a varying degree of fibrosis develops. Respiration, however is only rarely affected to such an extent that subjective discomfort appears but it is phonation which is made difficult or in some patients, impossible. The injuries mentioned are usually noticed from some weeks up to a year or more after the end of the therapy but also while therapy is given the patient may have appreciable laryngeal trouble dysphonia passing into aphonia for one or more weeks, pain in swallowing and now and then a painful cough The subjective discomforts in these patients could perhaps be reduced if the vocal cords were kept completely inactive during the time of radiation and up to about two months after i e if the patient was completely quiet, but as in this situation the patient would not be likely to follow such instructions, we have never tried it Instead we have found it reasonable to teach the patient to use the vocal cords as carefully as possible

METHOD

During 1966–1968 15 of the patients who were given radiation therapy against laryngeal cancer in the Department of Radiotherapy in Lund were simultaneously treated in the Phoniatric Clinic. In these patients, the radiation therapy was given by the same method and with the same radiation source The phoniatric treatment started with examination and registration of the patient, including recording of the voice. At the same time the patient was carefully informed of the difficulties to come and instructed in voice hygiene Except for the two cases mentioned below voice treatment was given only in parallel with radiation ther

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THE PLACE OF PHONIATRICS IN THE ORGANIZATION OF MEDICAL CARE

G Bjuggren

From the Department of Phoniatrics Sabbatsberg's Hospital Stockholm Sweden

The phoniatric organization must cover the whole range of speech and voice disorders. In Sweden, medical specialists, phoniatricians, must co-operate with logopedes. In addition to two years of studies in phoniatrics, the phoniatrician has acquired knowledge in otolaryngology (1 year), audiology child and adult psychiatry and clinical neurology (6 months each). Three years of university studies lead to a degree in logopedics. In the phoniatric clinic of regional hospitals, this team co-operates with other specialists and teams at the same hospital, as well as with other logopedes and other medical and social specialists in smaller hospitals. School speech therapy has its own organization.

Phoniatric organization, like any other kind of organization, is built up of vertical and horizontal relations among a number of different elements.

As usual, the patient is the essential element. His legitimate claims must be met to the extent society places means at our disposal. It is up to doctors and other medical authorities to note these claims and find the best means of satisfying them. When planning the organization of a single branch of medical care, scope is restricted by the manner in which medical care in general is organized and planned in the country.

Phoniatric disorders are disturbances of language speech and voice. These vary greatly in aetiology pathogenesis and complexity of symptoms. They must be treated by specialists in both medicine and pedagogics. Medical science is primarily represented by otolaryngology child psychiatry neurosis psychiatry and clinical neurology. In Sweden as in Finland, our field has its own speciality—phoniatrics.

New Swedish regulations for those wishing to acquire competence in phoniatrics have recently been announced. The training requires 1/2 year of studies in each of the subjects mentioned, except for otolaryngology which, as is proper takes up 1 year in addition to 1/2 year of audiology. Two years of study are required in the main subject, phoniatrics. The pedagogic form of treatment is practised by voice and speech therapists. There are two separate, parallel lines of study in Sweden. One is a 3-*year* academic programme, whose latter half is placed in a department *of medicine, and which ends with a degree in* logopedics. The other line is a special teaching line at the Teachers College for Advanced Studies (*Lärarhögskolan*). *It has* a 6–7-year period of training with only 1 year dealing with logopedics. This schooling leads to an appointment as a speech pedagogue at a school speech clinic.

Phoniatrics has been a medical speciality in Sweden for several decades. As I have been led to understand, we are indebted to the initiative and far-sightedness of Professor Gunnar Holmgren for this. In Sweden, phoniatric disorders are a problem for organized medical care programmes. These programmes are administered by way of seven regions, each with a regional hospital in which all medical specialities are represented. Each regional hospital has a phoniatric clinic headed by a phoniatrician with logopedes as speech therapists.

In Swedish schools, phoniatric-logopedic activities are carried out in speech clinics. There

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THE MOVEMENTS OF THE TONGUE AND THE SOFT PALATE DURING ARTICULATION AND THE SWALLOWING PROCESS

Siems Siemssen, Arthur Boberg and Nils H Buch

From the Department of Otolaryngology Copenhagen County Hospital Glostrup the Radiation Therapy Centre and the Department of Plastic Surgery the Finsen Institute Copenhagen, Denmark

The film shows a male patient who had an extensive cancer of the left tonsil After extirpation of the tonsil, partial resection of the cheek the left part of the mandible and the maxilla, the movements of the tongue and the soft palate were still perfectly normal, and the actual case was—because of the special circumstances—suitable for a demonstration of these movements.

In technicolor and talking pictures the patient demonstrated open and narrow vowels in connection with different consonants. The difference between orals and nasals is shown.

The motor details are demonstrated at normal speed and in slow motion. The reactions of the above-mentioned organs in the act of swallowing are displayed in special recordings.

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cal steps must be taken in many instances. However the phoniatrician is competent to administer limited therapy in the aforementioned medical specialties, which is why collaboration with practitioners of these specialities is necessary

In the case of certain disorders it is no longer a question of therapy in the customary sense, but of habilitation and rehabilitation, mainly in respect to vocational training, but also in order to induce the patient to be able to cope on his own. Ultimately phoniatricians and logopedes must actively organize co-operation with occupational and social therapists of different kinds so that aphasics, for example are able to utilize their resources for communication and contact after the completion of therapy

With decentralized care, in which the phoniatrician, for obvious and practical reasons, cannot be consulted except in individual cases, as well as in teams for the care of the aforementioned special forms of chronic illness or handicap in which, for the same reasons, the phoniatrician cannot participate directly the tasks of the phoniatrician must be distributed between the logopede and some representative of the medical speciality most appropriate to the case in question. It is obvious that the logopede, who must represent the entire field in such circumstances, must bear a heavy responsibility It is also obvious that the better the logopede's insights into the pedagogic and medical aspects of the field, the better prepared is he to accept that responsibility

It is conceivable that many of my colleagues might immediately fear the prospect of charlatanism. My opinion is that the risk of charlatanism is best checked by knowledge. Another aspect of the problem might be that the logopede in this way could make the phoniatrician superfluous. However hitherto my own logopedes have never questioned my continued existence as a phoniatrician.

DISCUSSION

U Sirala If phoniatry becomes a "super specialty" in otolaryngology it will be difficult to get young doctors interested in this field of medicine because the long study time. Already now we have difficulties in getting enough physicians in phoniatry If we were lucky enough to get these "super-specialists they would mostly be interested in otology because of the better income from it. The other specialty—phoniatry—would suffer from this.

In Finland, rehabilitation of patients is officially accepted as part of the function of a hospital. In the rehabilitation of oto-rhino-laryngological patients the phoniatrician's contribution is very important and useful. A speech therapist should never work alone, only in co-operation with a phoniatrician in order that good results can be achieved.

A Pretzmann Jensen Are there physicians in Sweden and Finland who are educated as specialists in phoniatrics without having recognition as specialists in otology?

G Bjuggren (Reply to Sirala and Pretzmann) We may argue in favour of a lot of different subjects and their merits as necessary requirements in the training of future specialists in phoniatrics. Nevertheless, we have to select and give preference to subjects of greatest importance in acquiring competence as a specialist. Otolaryngology is undoubtedly of basic importance to a phoniatrician. I am the only phoniatrician in Sweeden with complete otolaryngological training. There is no doubt that I can really benefit in my work as a phoniatrician as the result of my full competence as such a specialist. One year of training in otolaryngology may be a short time. In my opinion, however the two years of training in phoniatrics itself ought to be partly done in close co-operation with the staff of the otolaryngological clinic of the training hospital and, thus, be a good supplement to the required one year of training in otolaryngology and

is only good to say about these activities as such. But organizing a field as small as this as two independent pyramids, as we have seen in the two parallel educational lines men tioned previously in such a small country strikes me as being ill advised It is only thanks to the co-operativeness of speech therapists and their interest in the medical aspect that there are any chinks at all in the bureaucratic ally massive walls of the schools. A few years ago I passed on to responsible authorities in the Swedish Board of Education some of my critical views as well as a number of construc tive proposals I can only hope that they are paid some notice

Phoniatric activities in a medical care region have their centre in the phoniatric clinic. How ever a region is relatively large and, therefore many patients live at a considerable distance from the clinic. Thus, logopedic therapy which generally requires as many as 20–30 visits, can create considerable disturbances in a patient s regular activities For other patients, hemiple gics for example the many long and frequent journeys—perhaps delayed by waiting—can give rise to major physical and emotional prob lems. Providing hospital beds for such cases would be sheer extravagance One good solu tion might be for Mohammed to go to the mountain i. e to decentralize Of course this conflicts with the modern principle of placing medical care on an equal footing with industrial production in large units. But I would person ally regard this as a dangerous development if it could lead to compromising an indivi dual s demand for human consideration.

Therefore logopedic activities should be de centralized to a certain extent by establishing logopede appointments at a number of smaller hospitals.

Whenever some disturbance of language, speech and/or voice occurs in conjunction with any kind of chronic illness or handicap requir ing special care the most practical solution is, as a rule to transfer phoniatric logopedic treat ment to the institution at which the patient is receiving care. This applies, inter alia to child ren with defects of the palate, with cerebral palsy or mental retardation The care of deaf patients or those with impaired hearing is managed by special organizations. Intimate col laboration between these organizations and the phoniatric clinic is, in principle, natural and proper but, in practice, not always so easy to achieve

Phoniatricians and logopedes in the phonia tric clinic constitute a team in which the pho niatrician is primarily responsible for examina tions and diagnoses and the logopede for therapy A number of other members could, of course, be included in the team. psycholo gists, pre school teachers, occupational thera pists, etc.

I lectured on the work of phoniatricians and logopedes in, among other places, Copenhagen a number of years ago and in Oslo a little more than a year ago.

The examination made by the phoniatrician is, as in any other medical examination, gen eral as well as focused on special body systems and functions. This is quite self-evident and is reflected in the training of the phoniatrician. This training integrates the various medical disciplines I just mentioned. In every case, the phoniatrician carries out ear nose and throat examinations special emphasis is given to the larynx in cases involving the voice A more or less limited neurological examination is fre quently called for In the case of retarded speech development, the examination could take on the character of a child psychiatry study The history is essential in all medical examina tions, but is of especial significance in most phoniatric disorders. Psychological and so cial factors will emerge at the history taking. Voice disturbances very often have a psycho genic origin, and it is generally the social han dicap which brings the patient to the phonia trician In addition, evaluation of the patient s ability to function socially is generally a deter mining factor in the phoniatrician s therapeu tic decisions.

Even if treatment of phoniatric disorders is largely a question of logopedic therapy medi

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SHOULD PHONIATRY BE AN INDEPENDENT SPECIALITY OR A SUBSPECIALITY?

O H. Meurman

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The role and tasks of phoniatry are of topical interest all over Scandinavia. In this paper the tasks of phoniatry and the Finnish demands on the speciality in this discipline are considered from an otological point of view

In Finland, phoniatry is an independent speciality of medicine Recognition as a specialist in this discipline requires basically 2–2 / years experience in phoniatric work and 12 months in otorhinolaryngology In addition, the candidate must have worked for 6–12 months within the fields of child psychiatry neurology or psychiatry

The causes of voice and speech disorders may roughly be classified into peripheral, endocrine, central lesions and combined groups, and the treatment involved therefore ranges under different fields of medicine as follows:

Causes	Field of medicine
Peripheral	
Otogenic	Otorhinology
Rhinogenic	–
Laryngeal	
Oral	Plastic surgery
Dental	Dentistry
Endocrine	Endocrinology
Central	
Mental	Psychiatry
Neurological	Neurology
Combined	

However both from diagnostic and therapeutic points of view many of the peripheral causes are so intimately related to otorhinolaryngology that it is not possible to dissociate them from that speciality of medicine. Accordingly phoniatric disorders are, in my opinion, inseparably connected with otorhinolaryngology and they must therefore be diagnosed and treated in ear nose and throat clinics.

For this reason, I suggest that phoniatry should rank as a subspeciality based on a complete training in otorhinolaryngology and supplemented with extensive experience in phonetics, respiratory physiology endocrinology neurology and psychiatry

In this way phoniatry would become a branch of medicine providing improved possibilities both in clinical practice and research, and the phoniatrician would be able to give useful advice to the speech therapists and supervise their work.

DISCUSSION

B Fritzell I do not think there is really much disagreement except for semantic reasons. However the ability and training to perform operations could not be used as a criterion of independence. If so, neurology and internal medicine would not be considered independent. In the continued discussion, it is necessary to keep two things apart, viz. educational independence as a separate specialty on the one hand, and organizational independence on the other If we want to, we may compare it with a Department of General Medical Rehabilitation.

a half year in audiology The clinical relation of phoniatrics to otolaryngology and audiology is of corresponding importance Neverthe less, phoniatrics must maintain its own spe ciality content which has integrated parts of otolaryngology as well as of the other fields mentioned Such a difference is not essential as regards the aspects of organization On the contrary even if phoniatrics dares to run the commonly known risk of dependence on a large and powerful neighbour the existing connec tions are of real pragmatic value and should be developed even more.

Professor Siirala supposes that an otolaryngologist who intends to continue his studies in order to become a phoniatrician will abstain from his training when discovering that his income from phoniatric practice will be smaller Undoubtedly this has been and still is, the case in many instances But according to new principles in agreements concerning appointment as a medical doctor in Swedish hospitals, the financial difference between the two specialities will be compensated in future. As regards the possibility of logopedes replac ing phoniatricians, I have not expressed any decided opinion I have only called attention to a problem which is similar to another problem i Swedish medical care. This concerns experiments conducted in which highly qualified nurses take over some medical tasks from medical doctors. In my paper I have already mentioned psychologists and occupational ther apists as temporary or permanent members of the phoniatric logopedic team However in Sweden we have very good collaboration with clinics for child psychiatry and other specialities.

In Sweden, neurological and general rehabilitation clinics, respectively and clinics for long term diseases are attached to hospitals.

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From the Department of Otolaryngology University Hospital Turku, Finland

The role and tasks of phoniatry are of topical interest all over Scandinavia. In this paper the tasks of phoniatry and the Finnish demands on the speciality in this discipline are considered from an otological point of view

In Finland, phoniatry is an independent speciality of medicine. Recognition as a specialist in this discipline requires basically 2–2 1/2 years experience in phoniatric work and 12 months in otorhinolaryngology In addition, the candidate must have worked for 6–12 months within the fields of child psychiatry neurology or psychiatry

The causes of voice and speech disorders may roughly be classified into peripheral, endocrine, central lesions and combined groups, and the treatment involved therefore ranges under different fields of medicine as follows.

Causes	Field of medicine
Peripheral	
Otogenic	Otorhinology
Rhinogenic	–
Laryngeal	
Oral	Plastic surgery
Dental	Dentistry
Endocrine	Endocrinology
Central	
Mental	Psychiatry
Neurological	Neurology
Combined	

However both from diagnostic and therapeutic points of view many of the peripheral causes are so intimately related to otorhinolaryngology that it is not possible to dissociate them from that speciality of medicine. Accordingly phoniatric disorders are, in my opinion, inseparably connected with otorhinolaryngology and they must therefore be diagnosed and treated in ear nose and throat clinics.

For this reason, I suggest that phoniatry should rank as a subspeciality based on a complete training in otorhinolaryngology and supplemented with extensive experience in phonetics, respiratory physiology endocrinology neurology and psychiatry

In this way phoniatry would become a branch of medicine providing improved possibilities both in clinical practice and research, and the phoniatrician would be able to give useful advice to the speech therapists and supervise their work.

DISCUSSION

B Fritzell I do not think there is really much disagreement except for semantic reasons. However the ability and training to perform operations could not be used as a criterion of independence. If so, neurology and internal medicine would not be considered independent. In the continued discussion, it is necessary to keep two things apart, viz. educational independence as a separate specialty on the one hand, and organizational independence on the other If we want to, we may compare it with a Department of General Medical Rehabilitation.

N Buch In Denmark the group working with speech therapy in public schools has strongly characterized the developments during the last few years. Communication problems between the speech therapists and doctors have made the work and its practical effect more difficult. While the working field has been widened, the scientific work on speech disorders has not progressed sufficiently and the limited medical engagement here has been important. A greater medical expertise in this field is essential if we like the teachers and psychologists, want to have a greater influence on this problem, the arrangement and the organisation. Young doctors interested in phoniatrics must be given a reasonable position and such conditions that they have an opportunity to show exactly this necessity of a medical effort, both in clinical and scientific work

Boberg I have no competence to speak here. As a speech therapist I just want to ask for help Until now every patient with speech, voice or language disorders has only been treated by speech therapists. We do not obtain sufficient knowledge during our training. In order to help the patients in the best possible way better knowledge and research are required, and in that field the members of the medical profession can help us.

O Meurman (Reply) In my opinion, the most important work of a phoniatrician is to clear up the aetiology and to establish the diagnosis. The therapy and rehabilitation follow after that. This is a common law in all medicine.

As long as a phoniatrician works in an ear clinic with continuous possibilities of consultations, his basic training in otolaryngology is perhaps not so important. When he starts to work independently outside the ear clinic the situation is entirely different. In diagnostic work it is very important to have a thorough training in otolaryngology

Acta Otolaryng. 263 137–138, 1970

DEOXYRIBONUCLEIC ACID CONTENT IN BRONCHOGENIC CARCINOMA

O Grenen

From the Departments of Anatomy and Otolaryngology University of Aarhus, Denmark

The DNA content in biopsy material of bronchogenic carcinomata was measured by a microspectrophotometric technique. The average content of DNA was considerably elevated as compared with the normal broncial epithelial nuclei. The number of polyploid tumour-cell nuclei was 10 times as large in squamous-cell carcinoma and adenocarcinoma as in oat-cell carcinoma.

The formation of the polyploid nuclei and their role in malignancy are discussed.

It is characteristic of tumour-cell nuclei that they have a high content of DNA, and that the values show a wide dispersion. In normal tissues the values are concentrated around a diploid mode, with a few nuclei within the range up to twice the diploid mode, owing to the DNA synthesis prior to mitosis. In tumour tissue, the values extend from a basal modal level, with many cell nuclei in the range up to twice that level, and often an appreciable number of values above the latter (polyploid cells)

Bronchogenic carcinomata are very suitable objects for the study of the DNA content, because the same organ harbours various histologically well-defined types of carcinoma, whose course and degree of malignancy are well known from clinical observations.

In this biopsy material the average DNA content in bronchogenic squamous-cell carcinoma, adenocarcinoma and small-celled anaplastic carcinoma was found to be much higher than that of the normal bronchial epithelium. The average DNA content was slightly lower in the small-celled anaplastic carcinoma than in the two other groups.

The measurements suggested that the distribution patterns of the nuclei of the three types of carcinoma differed, with only a small number of polyploid cells in the small-celled anaplastic carcinoma. It was found that the number of polyploid nuclei in squamous-cell carcinoma and adenocarcinoma was about 10 times as large as in the small-celled anaplastic carcinoma.

The formation of polyploid nuclei may occur after the synthesis of DNA by an inhibition of the splitting of the chromosomes or of their movements. In tissue culture, unfavourable growth conditions may result in the formation of certain substances which inhibit cytokinesis, and therefore give rise to the production of polyploid cell nuclei.

Provided that the vital processes are preserved, the polyploid cells are not as efficient as diploid cells in cell reproduction. In order to divide once, the former must synthetise more material than the latter This has also been shown experimentally

When polyploid nuclei are much more frequent in squamous-cell carcinoma and adenocarcinoma, which have a better prognosis than the highly virulent small-celled anaplastic carcinoma, this may mean that the two former tumour types provide less favourable growth conditions, causing inhibition of mitosis while the cells continue to synthetise DNA, resulting in the formation of these large dark nuclei with a high content of DNA.

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THE NOISE DOSIMETER FOR MEASURING PERSONAL NOISE EXPOSURE

S. Lagerholm and N G Toremalm

From the University Department of Otolaryngology Allmänna Sjukhuset Malmö Sweden

A pilot study of personal noise exposure measurements with the use of noise dosimeters is presented. The value of objective individual recordings regarding the intensity and the exposure time is emphasized. Unexpected daily variations were detected also among employees assumed to work in fixed noise-level environments. Objective measurements of intensity and exposure time completed by calculation of the frequency parameter seem more adequate than the previously used objective measurements of intensity and frequency completed by rough estimation of the time parameter

The dosimeters have also discovered great variations in the individual noise panorama following change from night to day shift or seasonal production fluctuations. Repair and inspection of factory machines involve also great individual increases in noise exposure.

With the dosimeters it was also possible to distinguish between three different groups of employees in the factory with regard to their exposure to noise So far it seems practical to allow noise exposure above the linear 85 dB level of 0.5 decibel hour per working hour (dBh/h), whereas an amount of noise exceeding 1.0 dBh/h is not tolerable unless adequate noise protectors are used Further investigations are necessary before definite prescriptions for the practical utilization of the noise dosimeters can be recommended.

Continuous observation as an aid in hearing-loss prevention can briefly be broken up into a general and an individual programme. *The general programme* includes good noise insulation of factory premises and suitable design of manufacturing machines, which must be checked by repeated conventional measurements of noise intensity and noise frequency The result of such "point measurements" can then be graphed as a noise-rating curve as shown in Fig. 1 These two parameters give an account of the noise panorama of the premises at fixed distances from the noise sources. It is not, however possible from these calculations alone to determine the level of unwanted noise at the ears of the employee There is also a third factor—the exposure time—which it has so far been possible to estimate only approximately

The individual programme for the observation of people exposed to noise has up to now mainly been based on the above-mentioned measurements of the premises, which have then been matched against sometimes very unreliable exposure-time estimations, and correlated to certain agreed risk *criteria*. Analyses of this type are finally completed by annual ENT examinations including an individual tone audiogram. Some places have recommended pre employment temporary-threshold-shift (TTS) determinations (Nixon *et al.* 1965) The value of this type of *examination* used as a prognostic test has, however been disputed by Opliger *et al.* (1960) and others.

Among the above mentioned measurements, the conventional analyses of intensity and frequency are the most reliable ones, whereas the earlier subjective exposure-time estimations have very often been a matter of controversy This is, in our opinion, due to the lack of methods for objective recording of the time para-

small-celled anaplastic carcinoma is due to its greater tendency to rapid growth and rapid metastatic spread and to its invasion of the pulmonary vessels.

If the polyploid cells can be taken as a manifestation of unfavourable growth conditions and a lower virulence it must be assumed that only relatively slight inhibition of the growth occurs in the small-celled anaplastic carcinoma as compared with squamous-cell carcinoma and adenocarcinoma, which is in good agreement with clinical observations.

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With the dosimeters it was also possible to distinguish between three different groups of employees in the factory with regard to their exposure to noise. So far it seems practical to allow noise exposure above the linear 85 dB level of 0.5 decibel hour per working hour (dBh/h), whereas an amount of noise exceeding 1.0 dBh/h is not tolerable unless adequate noise protectors are used. Further investigations are necessary before definite prescriptions for the practical utilization of the noise dosimeter can be recommended.

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meter This deficiency in the individual noise injury prevention programme led to the devel opment of the previously described noise dosimeter (Lagerholm & Toremalm 1966)

The aim of this investigation is to present a preliminary field survey using the noise dosi meters continuously on a group of employees in a can factory with very high noise levels. The results are then discussed in order to give preliminary recommendations regarding the practical utilization of the apparatus and also to test the significance of the method before using it as a routine in the social and technical noise prevention programmes.

METHODS

The theoretical considerations, as well as the clinical development and laboratory tests of the dosimeters, will be described (Lagerholm & Toremalm to be published) Therefore only a short summary will follow here. The dosimeter consists of a special microphone, a small transistorized linear amplifier a loga rithmic clipper a rectifier and a chemical integrator in which unwanted noise can be stored in the form of electric energy All components are contained in one plastic unit, so that the dosimeter can easily be worn in the chest pocket of an overall The sensitivity of the apparatus can be adjusted to any desired threshold level In this investigation, a linear 85 dB level was chosen as the zero line which means that noise with an intensity slightly above 85 dB on one or more frequencies is recorded automatically as a function of time. After a period of a day a week or a month the accumulated noise excess can be read off on a separate meter The stored quantity of noise has been calculated in a unit which we so far have called the decibel hour (dBh) One dBh per working hour (dBh/h) means that the wearer has worked continuously in surroundings with a noise intensity of about 86 dB at one or more frequency bands for one hour or at an equivalent higher intensity during a shorter period.

RESULTS

The actual can factory produced different types of noise with rather high intensities. Four different noise sources are shown in Fig. 1 The recommended norm for tolerable noise exposure—the N 85 line—is plotted on one of the curves. All noise sources in the factory had their maximum noise levels within the limits of the dosimeter microphone, i e. 500–8000 cps

Thirty four persons were included in the investigation which lasted for five weeks. The employees were occupied in different sections of the factory One group of workers was stationed near the same machine all day long, whereas a second group contained workers, foremen and engineers with more mobile and varied duties. The individual amounts of noise exposure, together with the mean values and scatter is shown in Fig. 2. It will be seen (to the left in the figure) that 10 persons were exposed to more than 1 dBh per working hour This is equivalent to a constant exposure to noise exceeding 85 dB Five were occupied at automatic stamping presses and four worked at printing presses The tenth man in this group was a body maker operator manufacturing beer cans. The second group (the middle of Fig. 2) was exposed to 0 5–1 0 dBh per working hour This group was more heterogeneous, containing workers from different sections of the factory In the third group (to the right in Fig 2) the noise exposure did not exceed 0.5 dBh per working hour The people in this group can be classed as low-risk cases and were often foremen or engineers. Owing to their mobile occupations and, as a rule, noiseless surroundings in their ordinary working rooms, the total exposure time was small but varied widely from day to day

From the total case material in Fig 2, four individual day by-day exposure curves are shown in Fig 3 a–d for closer analyses.

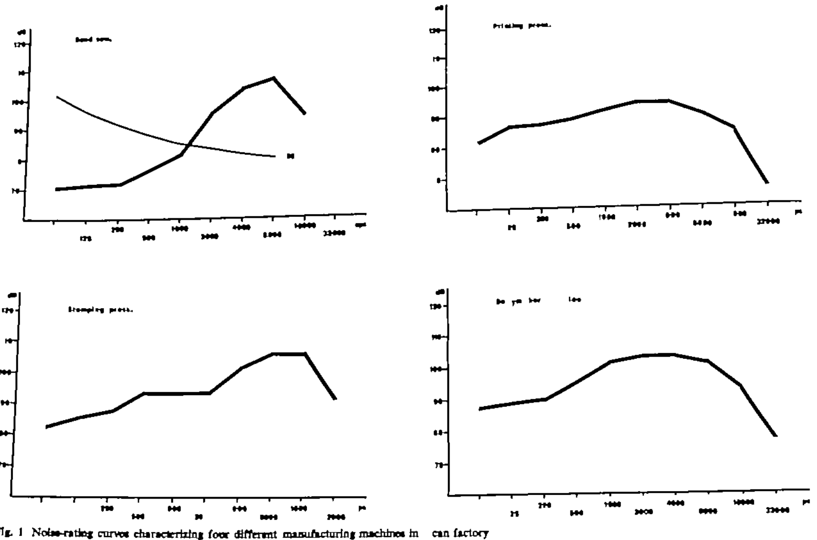


Fig. 1 Noise-rating curves characterizing four different manufacturing machines in can factory

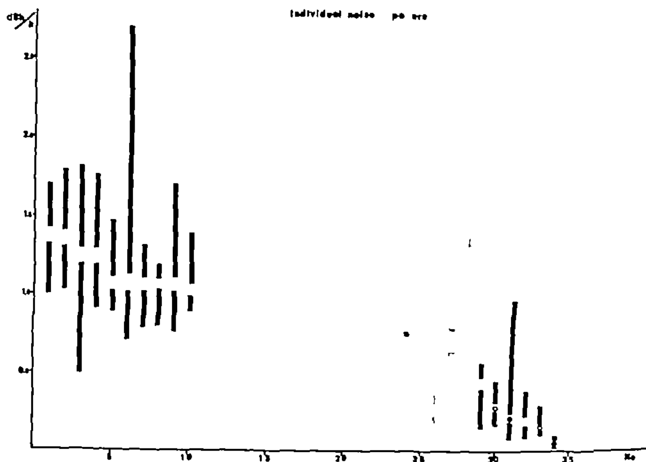


Fig. 2. *Individual* noise exposure for 34 employees recorded by the noise dosimeter. Mean values and scatter in dBh/h (decibel hour per working hour) during five weeks.

1 A. O (Fig. 3 a) is a 5 year-old employee. He has worked in the can factory since 1935 Throughout this investigation he was occupied at an automatic stamping press with a measured noise level of 90–100 dB (Fig. 1 bottom left). The dosimeter curve shows a mean value of 1.. dBh/h with a scatter of 0.9–1.8 dBh/h. The total exposure during 15 whole working days was about 160 dBh.

2. K H (Fig 3 b) is 34 years old. He has worked in another factory with high noise levels for 10 years before he entered the can factory Here he has been occupied at a body maker with a noise level of about 100 dB He had a mean value of 1 7 dBh/h and a scatter of 0.9–1 47 dBh h. The prominent rise on the 14th and 15th days was due to a change-over from night work to day work

3 N N (Fig 3) is 4 years old. He began in the can factory in 1953 and has always operated a printing press with a noise level of about 90 dB. He had a mean value of 1 05 dBh/h and a scatter of 0 76–1 70 dBh h The cause of the extreme rise on the 18th day is not exactly known, but may be due to machinery trouble. Occasionally metal sheet becomes jammed in a machine The distance to the noise source decreases during repair and the noise exposure increases.

4 R H (Fig 3 d) is fourth example of individual noise exposure detected by the noise dosimeter He is 25 years old and a typographer in his first year at the factory following four years in a printing office He belongs to the least exposed and had a mean value of 0 8? dBh/h and a scatter of 0.59–1.34 dBh/h. Also in this case however daily fluctuations can be seen, with an unexpected increase during three days.

The recordings were read by one person, who also gave necessary information to the workmen. The noise dosimeters were well tolerated by every individual and no problems appeared regarding the daily functioning and reading of the apparatus.

DISCUSSION

Previously it has been the rule to make *objective measurements of intensity and frequency* whereas the exposure time has only been briefly estimated This is effective only if the worker always has a permanent working place. This is, however not the usual condition in

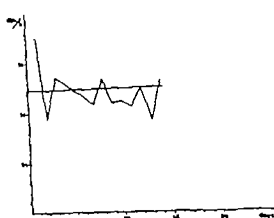


Fig. 3 a. Automatic stamping press operator (measured intensity 90–100 dBA). A. O. Mean. 1.23 Scatter 0.92 1.75

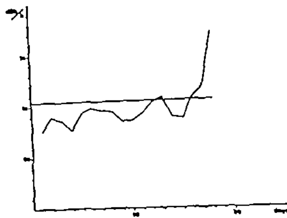


Fig. 3 c. Printing press operator (90 dBA). N N Mean: 1.05 Scatter 0.76–1 7

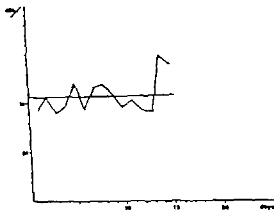


Fig 3 b. Body-maker operator (100 dBA). K. H. Mean: 1.07 Scatter 0 9–1.47

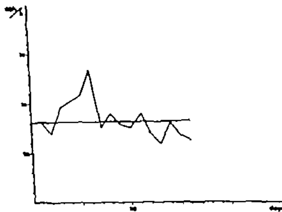


Fig. 3 d. Printing press operator (90 dBA). R. H. Mean: 0.82. Scatter 0.59–1 34

Fig. 3 Four individual noise exposure curves showing unexpected day-to-day variations (dBA/h).

modern industries, which is also seen in the present individual scatter (Fig. 3)

We have therefore preferred to make *objective measurements of intensity and exposure time* and to calculate the frequency parameter as it is not possible to obtain a total frequency analysis by means of a pocket-sized measuring apparatus. This is, in our opinion, not even necessary for the actual purpose, which is to mirror the day-to-day level of individual noise exposure. We have found that most ordinary industrial equipment and machines contain a maximum intensity hump somewhere in the frequency range 500–8000 cps. This is exemplified in Fig. 1 The finding has been the basis for the choice of an acceptable dosimeter microphone, which must naturally be small, reliable in operation, shockproof and insensitive to temperature (Lagerholm & Toremalm, in press) Thus, the dosimeters work independently of the position of the actual intensity hump within the above-mentioned frequency range.

The four individual examples (Fig. 3) include people who are very often considered to have a fixed working place. This conception

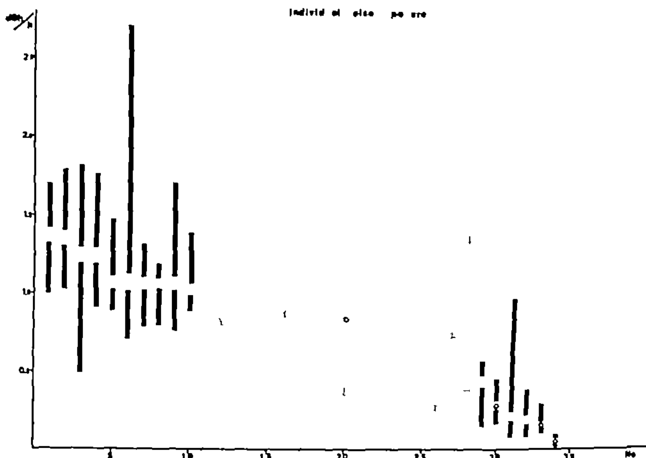


Fig. 2. Individual noise exposure for 34 employees recorded by the noise dosimeter. Mean values and scatter in dBh/h (decibel hour per working hour) during five weeks.

1. A. O (Fig. 3 a) is a 52 year-old employee. He has worked in the can factory since 1935. Throughout this investigation he was occupied at an automatic stamping press with a measured noise level of 90–100 dB (Fig. 1 bottom left). The dosimeter curve shows a mean value of 1.2 dBh/h with a scatter of 0.9–1.8 dBh/h. The total exposure during 15 whole working days was about 160 dBh.

2. K. H. (Fig 3 b) is 34 years old. He has worked in another factory with high noise levels for 10 years before he entered the can factory. Here he has been occupied at a body-maker with a noise level of about 100 dB. He had a mean value of 1.7 dBh/h and a scatter of 0.9–1.47 dBh/h. The prominent rise on the 14th and 15th days was due to a change-over from night work to day work.

3. N. N. (Fig 3 c) is 42 years old. He began in the can factory in 1953 and has always operated a printing press with a noise level of about 90 dB. He had a mean value of 1.05 dBh/h and a scatter of 0.76–1.70 dBh/h. The cause of the extreme rise on the 18th day is not exactly known, but may be due to machinery trouble. Occasionally a metal sheet becomes jammed in a machine. The distance to the noise source decreases during repair and the noise exposure increases.

4. R. H. (Fig 3 d) is fourth example of individual noise exposure detected by the noise dosimeter. He is 25 years old and a typographer in his first year at the factory following four years in a printing office. He belongs to the least exposed and had a mean value of 0.8? dBh/h and a scatter of 0.59–1.34 dBh/h. Also in this case, however, daily fluctuations can be seen, with an unexpected increase during three days.

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INSTRUMENTATION FOR ACOUSTICALLY EVOKED POTENTIALS USING A PHOTOGRAPHIC AVERAGING TECHNIQUE

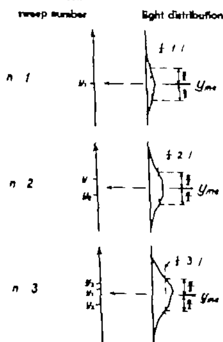
E. B. Neergaard and S Hardy

From the Department of Otolaryngology University Hospital, Aarhus, Denmark

The measuring method incorporates photographic device to obtain an average recording of the vertex potentials. The patient is stimulated with pure tones just as in conventional audiometry: the repetition rate is one stimulus per 10 seconds. The vertex potentials are recorded from skin electrodes connected to diff ferential amplifier and displayed on an oscilloscope. The superimposed traces of repetitive responses are transferred to polaroid film via special optical system, and the recording thus obtained reveals the average of the evoked potentials.

The exhibition contains the original instrumentation for optical averaging technique as applied in ERA at Aarhus Kommunehospital. The aim in the instrument construction has been to provide a simple and reliable clinical set-up without the use of expensive electronic computers. A further feature which has been gained in practice is an unusual immunity to noise peaks.

Arithmetic Mean



Median

In psyiologic measurements the media will often be preferred to the arithmetic mean.
Optically it may be produced so

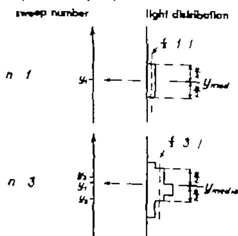


Fig. 1. Diagram to explain the formation of mean and median of several traces displayed on an oscilloscope by optical technique

must obviously be revised since many of our subjects with fixed working places demonstrated great individual fluctuations in noise exposure from day to day It may be said that today there are practically no workers with a constant level of noise exposure Thus to make use of approximate exposure-time estimations for later correlation to agreed norm tables is a questionable procedure even if it is the only one so far available.

Knowledge of daily variations is of special value during the introduction of new workers to a factory and the installation of new machines. The dosimeter readings are also valuable as indicators of the need for adequate noise protection.

Great variations in the noise panorama appear when workers change from night to day shift, to follow different production schedules This can be seen in Fig 3 b The same effect has also been detected in seasonal production fluctuations A third factor which may easily be forgotten is the many interruptions in the daily routine They can be of positive nature (rest breaks) or negative (e g. repair and inspection of machines) A short increase of 50 per cent is not uncommon as seen from Fig 3 c.

It is not possible to allow for such factors with the old methods. It would therefore seem to be more satisfactory in the future to follow the noise-exposure variations of every individual continuously This can easily be done with the dosimeter

Seen from a prophylactic point of view it is also possible to distinguish between at least three different groups of employees in a factory with regard to their exposure to noise (Fig. 2). If an individual observation is made for the permanent staff in a factory say monthly it is possible to concentrate different prophylactic measures to the most exposed subjects. This increases the efficiency and reduces the cost of a rational noise-prevention campaign.

It is not possible today to recommend definite criteria for using the dosimeter The values given in Fig. 2 seem, however suitable for the present It will be necessary to study different groups of workers in different types of industry for several years, and to correlate the values obtained by the dosimeter with known point measurements and with employee audiograms It should then be possible to sum up the total noise-energy load on a single ear and to correlate the figures obtained with audiograms and possible hearing losses. A list of individual noise-exposure figures can also be made and used for different medical and sociomedical purposes. Special investigation programmes have been started in order to gain more experience in this field.

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Acta Otolaryng. 263 147–154 1970

A SURVEY OF NON-TUMOROUS LESIONS OF THE SALIVARY GLANDS

H. Diamant and B. Enfors

From the Departments of Otolaryngology University Hospital Umeå, and Söder Hospital Stockholm Sweden

Introduction (Diamant)

The title of this lecture is not fully adequate to the subject. In the first place, the purpose is not to provide complete clinical survey but rather to concentrate on sialoadenitis and sialoses. In the second place, some other conditions of non-tumorous nature are touched on only lightly. This paper is the product of close co-operation between Docent Enfors and myself. I shall devote myself to a presentation of the different lesions, while Docent Enfors will report on diagnostic techniques and methods of treatment.

Diseases of the salivary glands are classified as shown in Fig. 1. Fig. 2 gives breakdown on the basis of sialoadenitis and sialoses. These conditions are of interest as regards both diagnosis and treatment. W shall, moreover discuss secretion disturbances, but trauma, strictures, etc. will not be considered, and tumours will be reserved for subsequent lecture.

Classification
1 Disturbance of secretion
2. Trauma
3. Benign stricture
4. Sialolithiasis
5 Sialadenitis
6. Sialosis
7 Tumour

Fig. 1 Lesions of the salivary glands.

Sialadenitis
a. Acute suppurative parotitis
b. Chronic recurrent parotitis
c. Specific infection

Sialosis
a. Collagen sialosis
b. Sarcoidosis
c. Hormonal disturbance
d. Asymptomatic parotid enlargement

Fig. – Sialoadenitis and sialosis of the parotid glands.

Examination techniques (Enfors)

The diagnosis in cases of non-tumourous lesions in the salivary glands is generally not difficult. By means of the case history inspection and palpation one can generally arrive at a provisional diagnosis which can be confirmed by further examinations. The inspection should include—and I must emphasize this—inspection of the appearance of the saliva. By massaging the salivary glands and their excretory ducts saliva can be expressed through the orifices. In any case, it is generally easy to massage saliva out of the parotid glands. However from the submandibular glands it is less easy and there one must often stimulate secretion by giving the patient a mouth-wash with a few millilitres of 6 % citric acid solution. Such stimulation is, moreover always valuable as the amount of secretion response indicates the functional condition of the glands.

The special examinations may be classified in three groups (Fig. 3).

A. Anatomical	
1 X-ray	*Without contrast*
	Sialography
2. Biopsy	Aspiration with thi needle
	Excision of tissue
B. Functional	
1 Secretion	Sialometry
	Chemical analysis
2. Scintigraphy	
C. Bacteriological	

Fig. 3 Laboratory examinations of the sal vary glands.

A dummy patient is used as a source of signals, which through an EEG pre-amplifier are displayed on two separate oscilloscopes. The reason for using two oscilloscopes is to demonstrate two alternative procedures to obtain optical averaging.

One oscilloscope is provided with a very special camera which simultaneously from the single traces on the screen produces three different types of recordings. The top recording is an ordinary photographic picture of the single traces superimposed. Below that a recording of the traces transformed optically in such a way that the arithmetic mean of the traces appears. At the bottom similarly there is a recording which gives the median.

The second oscilloscope has an ordinary polaroid camera, and the optical effect necessary for the production of the mean or median relies upon addition of a high frequency auxiliary voltage to the displayed ERA signal.

Both procedures utilize a controlled light dispersion where each point of the trace is transformed into a vertical line segment with a defined light intensity distribution

At the exhibition it was shown how this is done in practice, and some of the theory was illustrated Fig. 1 is a reproduction of one of the plates.

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A. Anatomical
- 1. X-ray — Without contrast; Sialography
- 2. Biopsy — Aspiration with thin needle; Excision of tissue

B. Functional
- 1. Secretion — Sialometry; Chemical analysis
- 2. Scintigraphy

C. Bacteriological

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Chemical analysis of the saliva as yet plays an unimportant role in clinical work. Our knowledge of the secretion of various substances by diseased glands is too scanty. However, it is probable that chemical techniques can be further developed.

It is open to discussion whether salivary-gland scanning should be included with the anatomical or with the functional examinations. Scanning provides information as to the size of the gland, but it is mainly of value as a functional test (Figs. 6 and 7). The radioactive isotope technetium[99m], which was introduced in the early 1960s, concentrates in the salivary glands, among other organs, a circumstance which permits salivary-gland scanning. One to six millicuries of the isotope are given intravenously. The isotope is secreted with the saliva, and it is therefore necessary to administer atropine before the examination to reduce salivation. Failure to administer atropine is probably the reason for the poor quality of most of the salivary-gland scans reported in the literature. Our experience is not yet very wide; nevertheless, the approximately 120 scans carried out at Södersjukhuset (Stockholm) where the technique has been developed together with M. Lind and B. Söderborg, *indicate* certain relationships between isotope uptake and disease in the salivary glands.

Bacteriological examination of the saliva is of lesser importance.

Diagnosis (Diamant)

Acute purulent parotitis is becoming commoner, probably because of the increasing number of operations on patients who are poor risks. This automatically causes an increase in the number of cases of acute parotitis. The patients are often in a very bad condition. In infants, however, acute purulent parotitis is less dangerous.

Chronic recurrent parotitis accounts for a very large proportion of our cases and can be diagnosed by using the methods specified by Enfors. This condition is characterised by acute episodes, invariably followed by a more or less pronounced swelling which sometimes disappears during quiescent intervals. The patients do not usually complain of dryness in the mouth because only the parotid glands are affected. Both roentgenological and sialometric changes are found bilaterally, even in cases where the patient has pain only on one side. Very often characteristic changes are found even in children. Burchinzki, in Poland, has collected a series of over 200 cases of chronic recurrent parotitis in children, diagnosed by means of sialography.



Fig. 6. Salivary gland scanning. Normal picture

And so we come to the sialoses. I shall not go into controversial questions, such as the dividing lines between sialoadenitis and sialosis, and the terminology proposed by various authors, but shall start right away with the commonest sialosis—namely, the collagenous. Very often the lesion of the parotid glands is part of the Sjögren syndrome. These patients complain mainly of xerostomia. Pain is seldom



Fig. 7. Scanning picture showing no uptake in the right submandibular gland. (Chorda tympani previously cut).



Fig. 4 Normal sialography of the parotid gland.

Roentgenographic study is a well tried method Non-contrast pictures are useful only for detection of salivary stones which are opaque while sialography provides a good picture of *the internal morphology of the glands* (Fig. 4) The commonest changes are those in the calibre *of the excretory ducts* and the *sialectases* There has been some discussion as to whether sialectases consist of preformed dilatations or whether they occur in connection with the sialography itself Ericson's study (1968) clearly *showed them to be preformed dilatations*

Either aspiration or ordinary biopsies may be taken *In aspiration biopsies the gland is* punctured with a fine needle and cell particles are sucked out. This is a very valuable examination when carried out by an experienced cytologist—*indeed* in most cases it is as reliable as histopathological examination It has been alleged that there is some risk of salivary fistulae with excisions for biopsies, but there is *no risk if the correct technique is employed.* Where a tumour can be suspected, however the latter method should not be used.

Salivary-gland function is determined mainly by means of sialometry which provides a quantitative record of the secretory capacity of the salivary glands. The saliva from the *parotid glands is collected separately from* each gland by a suction pump and collection chamber which is placed over the openings of Stenson's ducts. As a result of the secretion pressure the saliva runs out its volume being recorded by a photo-electric count of the number of drops. The secretion from the *submandibular glands must be collected by cannulae* inserted into the Wharton ducts Salivary flow is recorded both when the patient is at rest and when stimulated Stimulation can be *achieved* by various methods. Intravenous infusion of acetyl beta-methylcholine results in a brief but copious secretion of saliva (Fig. 5) *Pilocarpine may* also be used It produces a salivary secretion of longer duration. The dosage and rate of infusion must be calculated precisely *which can be done by means* of an infusion pump Salivary secretion can also be stimulated by gustatory means—i e with a 6 % citric acid solution in the mouth.

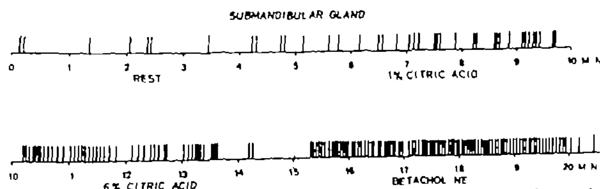


Fig. 5 The parotid secretion at rest after stimulation with 1 and 6 % citric acid and after stimulation with acetyl-beta methylcholine intravenously

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severe and there is not much enlargement of the salivary glands although this is sometimes the symptom that causes the patient to visit a physician In many cases, the patient develops no enlargement of the salivary glands and is therefore not referred by the rheumatologists In Umeå, however we have had an opportunity to see a number of the cases now under discussion thanks to close co-operation with the rheumatological department and also to the fact that one of our colleagues, Docent Ericson, of the Faculty of Dentistry (Tandläkarhögskolan) has taken a particular interest in the relationship between sialography sialometry and dryness" in the so-called Sjögren syndrome These cases were diagnosed by means of positive Rheuma-tests in conjunction with marked roentgenological changes in the salivary glands. They have moreover in more than a few cases completely inhibited salivary secretion Using fine needle biopsy a very highly trained cytologist can distinguish between chronic recurrent parotitis and collagen sialosis However the only person who can do this with any degree of accuracy is probably Professor Seifert in Hamburg

Sarcoidosis, on the other hand, can easily be diagnosed with aspiration biopsy In this disease, pronounced roentgenological changes are relatively rare The patients seldom have xerostomia, but they sometimes suffer pain

Another interesting group is hormonal sialosis. In this group I include a number of different conditions in which hormone changes may play a role We examined a series of young girls with enlargement and slight tension in the parotid, but no other symptoms. History reveals changes in the menstruation cycle generally in the form of amenorrhoea. This group also includes patients with enlargement of the salivary glands associated with diabetes, and perhaps also the enlargement that sometimes occurs in older persons.

In the fourth group I include cases in which the patient has enlargement of the parotid gland but in which sialometry sialography aspiration biopsy and even routine biopsy are normal In such cases the salivary gland enlargement follows an asymptomatic course I am unable to say what the aetiology is.

I should here like to present some material collected over a period of six years During the first three years there were few cases, but in 1966–1968 the number increased (Fig. 8) It will be seen that rheumatoid sialosis chronic recurrent parotitis and asymptomatic sialosis are in a clear majority These data are being analysed from various viewpoints, and we hope eventually to publish them in book form.

Therapy (Enfors)

As regards treatment of non-tumorous salivary gland diseases, the parotitis category presents

	Sialadenitis				Sialosis							
	Acute inflam		Chronic rec.		Coll gen		Sarcoidosis		Hormonal		Asymptomat.	
	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀
1963		1		1								1
1964			2		1							
1965		2				6						2
1966	1	2	5	1	1	10	1		2	10	3	
1967		2	1	3		1				2	3	3
1968		1	2	3	1	3			1	4	2	6
	1	8	10	8	1	20	1	–	3	16	8	12
												Summa 90

Fig 8 Review of patients with sialoadenitis and sialosis admitted to the Department of Otolaryngology in 1963–1968

many interesting problems. Postoperative purulent parotitis is a serious disease with a high mortality rate. Antibiotics are usually given although the results are poor. When definite softening and fluctuation occur there is no doubt that incision should be made, but in other cases it is hard to say what should be done. In the literature there is a variety of recommendations, including large incisions, small incisions, early incision and a restrictive attitude towards incision. Personally I have tried all these alternatives as well as such radical measures as acute parotidectomy, an operation which is surprisingly easy in these cases, but which does not seem to change the prognosis.

Cases of chronic recurrent parotitis are often so mild as to require no treatment; but some patients suffer severe pain. Antibiotics are commonly used during acute attacks, the duration and intensity of which are seldom, if ever, affected thereby. X-ray treatment may alleviate the pain temporarily in some cases. Often, ligation of Stensen's duct results in marked improvement. Sometimes, the duct recanalizes and pain recurs, but even when the ligation is definitive, periods of aching and swelling may recur. Parotidectomy is another possibility, but then the whole gland and not merely the superficial part must be removed. If parts of the gland remain, the pain often recurs just as before operation. Unfortunately the facial nerve is in most cases tightly attached to the fibrotic gland. Parotidectomy in cases of chronic parotitis, is therefore technically much more difficult than when the operation is performed on a gland with a normal parenchyma.

As regards the sialosis, our choice of therapy is very limited. Some improvement can be effected in cases of collagen sialosis, if the basic disease also improves. This is particularly true of the erythematodes, in which during remission periods a normalisation of the salivary gland changes may be observed.

Cases of sarcoidosis rarely require treatment but, if indicated, it does not differ from the treatment of sarcoidoses in other organs.

When hormonal parotid changes occur it is, of course, the underlying hormone disturbance that must be tackled. Unfortunately this is a piece of wishful thinking that can rarely be realised. Asymptomatic enlargement is perhaps also hormonal. In practice, it can be reduced to a disfigurement.

Here I should like to comment on the symptom of dryness in the mouth as well as the opposite condition, drooling—that is, xerostomia and pytalism. When it is mainly the large salivary glands that show diminished secretory ability dryness is most marked at mealtimes. The patient must drink much and often during the meal. If it is the small salivary glands that are involved and the large glands are intact, the patient suffers dryness between meals. He is almost free from dryness while eating. However, usually both small and large salivary glands are affected. If the salivary glands have not entirely ceased functioning—a question which can be resolved by sialometry—some improvement can be achieved by stimulation of the secretion. Many patients feel better when they suck an acid caramel or any kind of pas-



Fig. 9. Niels Stensen.

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											Summa	90

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sialosis is a myo-epithelial sialoadenitis and sarcoidosis of the salivary gland is an epithelial sialoadenitis. Therefore, I wonder if it is correct to designate these two groups as sialosis.

H Engström. I do not think that 500–700 Rad involves a risk of cancer of the thyroid gland. I think people with experience in this field would not look upon 500–700 Rad as a dangerous dose. However one should perhaps be careful not to give it to patients under 50 years of age.

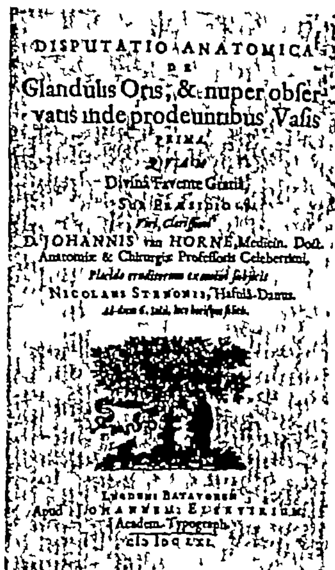
T Palva: It was mentioned by Dr Enfors that ligation of the parotid duct does not always give good results. I wonder if this is due to the presence of mucus-producing cells of the parotid glands, which do not always atrophy and may later cause even large mucus-containing cysts, which spread to the neck. Has Professor Diamant seen cases like this after duct ligature, or have all cases in his experience shown more or less permanent improvement of pre-operative symptoms?

The question of ptyalism, or sialorrhoea, was taken up by Enfors. This is, of course, a rare condition, but it can be very distressing to the patient. If we exclude all cases due to toxic cancer and concentrate on the patients in whom nothing abnormal is found, is there any known reason for this condition? Could it be due to hormonal imbalance, particularly in the cortico-adrenal system, the pituitary or perhaps, in the hypothalamus? A psychic factor might possibly also account for the symptoms. I should like to know if Dr Enfors has had any wider experience with these cases. Should, for example, hypnotic treatment always be attempted before resort is taken to more radical measures, such as auriculo-temporal nerve section or extirpation of the submandibular ganglion?

Sandberg to Enfors: Impaired removal of saliva was mentioned as an apparent cause of hypersalivation. I would like to report some cases that illustrate this type of hypersalivation, in which saliva is produced in normal amounts, but its elimination is disturbed. Two patients, both women, 43 and 63 years old, were referred to our clinic because of suspected hypersalivation. Both had been subjected to total gastrectomy with vagotomy for gastric cancer 2 and 16 months before admission, respectively. The patients complained of abundant saliva and of difficulties in swallowing both saliva and food, because swallowing took longer time than before. Physical examination revealed a moderate stagnation of saliva in the pyriform sinuses, but no pareses. Radiography of the hypopharynx, oesophagus and stomach showed normal conditions and oesophagoscopy revealed no tumour growth in the anastomoses. Intraluminal pressure recordings and recording of the deglutition pressures revealed pathological conditions with hypomotility and loss of peristalsis in the body of the oesophagus and increased tonus of the pharyngo-oesophageal sphincter. The disturbed function of the oesophagus was interpreted as a reflex inhibition of oesophageal motility after vagotomy. The production of saliva was not increased, but its elimination was impaired by disturbed oesophageal function. This produced symptoms of hypersalivation.

H Diamant (Reply to Eneroth): It is true that symptomatic enlargement of the parotid glands is fairly common in some tropic diseases, and also in pronounced starvation. Cases of this sort are not found in our series. Our patients with symptomatic enlargements have always been totally healthy people. We did, in fact, take biopsies from two of those cases and sent the specimens to Professor Seifert in Hamburg. The slides showed absolute normal pictures. None of the patients were alcoholics or had other similar vices.

(Reply to Engström) I agree that there are cases of the type you described with typical benign strictures of the Stensen duct. I am also sure that in these cases a dilatation of the stricture would give a good result. In my


DISPUTATIO ANATOMICA
DE
Glandulis Oris, & nuper observatis inde prodeuntibus Vasis
PRIMA,
Quam
Divina Favente Gratia,
Sub Praesidio
Viri, Clarissimi
D. JOHANNIS van HORNE, Medicin. Doct.
Anatomiae & Chirurgiae Professoris Celeberrimi,
Placidis eruditorum examini subjicit,
NICOLAUS STENONIS, Hafnia-Danus.
Ad diem 6. Julii, [illegible]

LUGDUNI BATAVORUM,
Apud JOHANNEM ELSEVIRIUM,
Academ. Typograph.
CIƆ IƆC LXI.

Fig. 10. Front page of Stensen's work on salivary glands.

tille If however secretion is greatly diminished and the mucous membranes in the oral cavity are atrophied throat tablets may cause discomfort. Another way to stimulate secretion is to put the patient on a small dose of pilocarpine—for example 1 mg morning and evening In certain cases the dose may without ill effects, be increased to 2 mg three times daily but as with this dosage many patients develop tachycardia some restraint is avisable

Drooling is another problem that is due partly to excessive secretion of saliva, but it is also necessary that the patient has difficulty in transferring saliva from the front of the mouth to the pharynx Drooling may occur in patients with injuries in the mouth, but it also occurs with cerebral injuries. About 10 % of children with cerebral paresis have troublesome drooling.

Extirpation of the submandibular gland on one side and division of the chorda tympani on the other may be carried out with favourable results. The pool of saliva which these patients have inside the lower lip diminishes and drooling decreases. Retroposition of the orifices of the submandibular ducts back towards the pharynx facilitates movement of saliva to the pharynx, which also has a beneficial effect in many cases. The exeretory ducts of the parotid gland may likewise be moved backwards, if necessary

It is clear that we have merely touched on the more controversial forms of therapy

Diamant: In conclusion, I cannot neglect this opportunity—especially since we are in Denmark—to pay tribute to Niels Stensen, later known as Nicolaus Stenonius, who, more than three centuries ago, gave a description of the salivary glands so meticulous that very little remained to be said on this subject (Figs. 9 and 10)

DISCUSSION

C M Eneroth: H Diamant, S Rauch and G Seifert are the three names which are especially associated with the classification of non-neoplastic enlargements of salivary glands. I have some questions to Diamant concerning his classification of the salivary gland enlargements. Sialosis or sialoadenosis (according to Rauch painless non-neoplastic, non-inflammatory salivary-gland enlargement) have been divided by Diamant into four subgroups. The groups 1 2 and 3 have been classified according to aetiology whereas the fourth is the so-called asymptomatic group. Do you have another name to suggest for this group? Idiopathic enlargement is also unsuitable, because neurogenic, metabolic and deficiency diseases (protein and vitamin deficiency) are included in this group. Morphologically the rheumatic

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SALIVARY-GLAND TUMOURS

CLINICAL PICTURE AND TREATMENT

T Leegaard and H. Lindeman

From the University Clinic of Otolaryngology Ullevål Hospital Oslo Norway

A brief account is given of the incidence and localisation of the various types of salivary-gland tumours. The pathology of these tumours is in many ways interesting and partially characteristic. The clinical picture of tumours with different localisations, the different diagnostic methods as well as prognosis and treatment of these tumours are considered. Finally the various forms of surgical and non-surgical treatment which are available are discussed.

Diseases of the salivary glands, and salivary gland tumours in particular constitute a well-defined chapter of pathology These tumours have many interesting characteristics, and have been increasingly studied and treated by otolaryngologists.

In the last decade, an increasing number of investigations in this field have been performed by Scandinavian otolaryngologist—investigations concerning diagnosis (sialometry aspiration biopsy), histology and pathology Salivary-gland tumours are comparatively rare, 0.2–0 6 % of all tumours, and approximately 2 % of all tumours of the head and neck.

In Norway all malignant tumours are reported in the Norwegian Radium Hospital. For the three years 1964 1965 and 1966 the following statistics have kindly been reported to us:

Table 1 *Malignant salivary-gland tumours*

	Men	Women	Total
1964	11	16	27
1965	17	19	36
1966	9	11	20

The incidence of all salivary-gland tumours in Norway is not known, but if the malignant ones are estimated to be 15 % then we should find about 180 salivary-gland tumours annually in the whole of Norway An important fact, shown by Eneroth (1965) should be mentioned. In the parotid, about 15 % of the tumours are malignant. In the submandibular gland, 50 % are malignant. Classification of the tumours according to pathology has for many years been very divergent, and consequently the evaluation of earlier literature is difficult. The classification used in our Department is very much like the one from the Radium-pathological Institute in Stockholm—published by Eneroth in 1964 (Table 2)

The whole of the tumour pathology cannot be considered and demonstrated in this short summary but we should like to stress our opinion concerning one particular tumour—the most common of them, the pleomorphic adenoma.

Recently as in the past, the pleomorphic adenoma has been put down as semi-malignant.

Table 2. *Classification of tumours*

Mixed tumour
Papillary cystadenolymphoma
Oncocytoma
Misc. benign tumours
Muco-epidermoid carcinoma
Adenoid cystic carcinoma
Acinic-cell carcinoma
Mucus-producing adenopapillary carcinoma
Trabecular adenocarcinoma
Solid anaplastic adenocarcinoma
Misc. malignant tumours

experience these cases are fairly unusual I have seen very few of them

The ligation can always be done before a major operation like parotidectomy

(Reply to Palva) Of course, there is a risk that a ligation in a case with too much secretion will lead to a collection of mucus or saliva in the duct behind the ligature I have seen this happen two or three times. It is not a great problem In cases with normal secretion I think that a dose of 500–700 Rad can solve the problem and stop the secretion for some time and thus make the ligation more likely to succeed.

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The recurrences are due to incomplete re moval of the tumour which has no real capsule but is not infiltrating or they may be due to the removal itself by dispersal of tumour cells *in the field of operation* *Furthermore* several investigations have shown that the recurrences are not more malignant that the original tumour If there is malignancy in the recur rence a reappraisal of the primary tumour will nearly always reveal the same picture there

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On the other hand, slow growth does not of necessity imply only a benign tumour Inspec *tion and palpation are important.* A pharyngeal extension of the gland could be inspected in the tonsillar region. Colour changes are seen in haemangiomata. Note if the surface is smooth tuberous, fluctuating, hard etc. *Pain* need not point towards malignancy A benign tumour located in the deep part can sometimes give a painful mastoid process.

In our experience facial paralysis is seen only on very rare occasions, except in far advanced cases. It should be remembered that a malignant growth can *circumvent a nerve* branch without causing nerve symptoms.

Sometimes a tumour in the deep portion of the gland can increase to such an extent that the superficial part is greatly compressed and the tumour is falsely considered to be su perficial Such a tumour will displace the facial nerve laterally stretch it and produce an abnormally ascending trunk which can easily become injured if the true situation is not realised On the whole, we should like to stress as *most important the clinical investigation In our* clinic we are of the opinion that a suspicious

lump or a probable tumour in this region should always have the surgical treatment necessary for a tumour

However other methods should sometimes be considered to confirm the diagnosis, if possible, and to clarify the situation. So, which are these methods? Radiography and sialography have, to us, given little help We do not think that these methods give much information in addition to the clinical findings. Sometimes, a chronic infection can give a picture very similar to that of a tumour

We have not used *schichtgraphy* for tumour diagnosis, but this method obviously provides a possibility of disclosing the function of the gland.

Aspiration biopsy is much favoured in some places, especially in Sweden. In Norway the pathologists have been more reluctant, partly because they feel that the cytological diagnosis is far less decisive than with the whole specimen, and partly because they fear possible growth from tumour cells lost during aspiration. This last objection does not seem to be valid, and further information of aspiration biopsy will no doubt come forth later in the discussion.

We do *not* do a regular biopsy pre-operatively Obviously there are too many risks associated with the opening of such a tumour We sometimes use a freeze biopsy but, on the whole, we prefer ordinary pathological examination of the specimen, followed a few days later by radical surgery if the postoperative pathology demands it. The opportunity then exists also to inform the patient of possible disfiguring results. We do not think it justified to damage the facial nerve without the patient's knowledge of this necessity An anastomosis, or transplantation, can be done to minimize the defect, but we at least, cannot guarantee the result, particularly if we think that postoperative roentgen treatment is necessary

However careful the clinical evaluation and the additional investigations are, difficulties may arise, as the following case history shows.

A woman, 60 years old, had for many years had a chronic parotitis with numerous exacerbations. She was admitted to our department because she had, for a few weeks, had a new painful swelling of her parotids. The skin over the sore swelling was inflamed, and purulent secretion was seen from the orifice of the duct of Steno.

Sialography demonstrated destruction of the glandular canal system. Total parotidectomy was thought necessary and in the centre of the fibrotic, chronic affected area, we found tumour an adeno-carcinoma. Histology demonstrated typical tumour cells in the ducts.

The *treatment of choice* of a salivary gland tumour is surgery This must be radical, i. e. the tumour must be removed together with all the glandular tissue covering it. Special attention must be paid to this rule in the most *common of all the salivary-gland tumours, the* pleomorphic tumour of the parotid, which, although being benign, has no real capsule of connective tissue. Mere enucleation should be considered a serious mistake

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Is neck dissection a must" in malignant salivary-gland tumours? We do not do it routinely only when suspicious lymph nodes can be *felt*. Roentgentherapy may be useful, perhaps chemotherapy as well. In some cases of cylindroma with recurrence we have observed more effect than we hoped for but, on the whole, salivary-gland tumours do not seem to react favourably to roentgentherapy

Within a limited time it has only been possible to review some points about the salivary gland tumours—points which we find are of importance. We hope the following discussion will amplify and enlarge our contribution.

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The *treatment of choice* of a salivary-gland tumour is surgery This must be radical, i.e the tumour must be removed together with all the glandular tissue covering it. Special attention must be paid to this rule in the most common of all the salivary-gland tumours, the pleomorphic tumour of the parotid, which, although being benign, has no real capsule of connective tissue. Mere enucleation should be considered a serious mistake.

During the operation it is very important to avoid injury to the tumour Rupture and dissimmation of tumour particles will give rise to multiple recurrences, and they are very difficult to deal with. How radical ought the operation to be? Should total parotidectomy always be done, or is it sufficient to remove the superficial portion if the tumour is located therein? Redon advocated total parotidectomy based on the assumption that multiple origins are always present in pleomorphic adenomata. Very few seem to adhere to this assumption any longer

Is neck dissection a must in malignant salivary-gland tumours? We do not do it routinely only when suspicious lymph nodes can be felt. Roentgentherapy may be useful, perhaps chemotherapy as well. In some cases of cylindroma with recurrence we have observed more effect than we hoped for but, on the whole, salivary-gland tumours do not seem to react favourably to roentgentherapy

Within a limited time it has only been possible to review some points about the salivary-gland tumours—points which we find are of importance We hope the following discussion will amplify and enlarge our contribution.

This is probably due to its tendency to recurrence, formerly often seen with these tumours. Another reason may be the postulation that *the tumour becomes more malignant with each* recurrence. A number of recent investigations have shown definitely we think that the word semi-malignant in this connection at least, should be abolished

*The recurrences are due to incomplete re*moval of the tumour which has no real capsule but is not infiltrating, or they may be due to the removal itself by dispersal of tumour cells in the field of operation Furthermore several *investigations have shown that the recurrences* are not more malignant that the original tumour If there is malignancy in the recurrence a reappraisal of the primary tumour will nearly always reveal the same picture there

The distribution of pleomorphic adenomata in the various salivary glands is, according to Rauch (1959) 84 % in the parotid 8 % in the submandibular gland, and 8 % in the remaining salivary glands, the lacrimal glands and the skin. *If we include all tumours,* 75–80 % are found in the parotid 10–15 % in the submandibular gland 2 % in the sublingual gland and 4 % in the oral cavity and elsewhere in the body

As far as the oncogenesis is concerned, we should only like to mention the conclusion drawn by Mylius in his article of 1960 The salivary-gland tumours are all developed from mature salivary gland tissue Tumours consisting more or less completely of myo-epithelium including the pleomorphic adenoma, originate from the interlobular ducts in the large salivary glands, or from "the neck zone" in the smaller ones The resemblance observed between some salivary-gland tumours and tumours of the lacrimal glands, the sebaceous glands and the mammary glands is due to one common factor *the myo-epithelial cell*

SYMPTOMATOLOGY

We have already mentioned that by far the greatest number of tumours are found in the parotid and we think it proper in a brief review to speak mainly of the symptoms of the parotid tumour The greater part of these tumours originate in the superficial and caudal part of the gland and most frequently the presenting symptom is a lump in the region of the ear We think it is a good practical rule to consider every "lump" every tumour thus *localised,* as a probable tumour of the parotid. Only by thinking in this way can an adequate treatment be assured Too often these tumours are still mistreated "I thought it was only a simple superficial tumour"—and consequently the removal will not take place in a manner necessary to prevent recurrence The symptomatology is, on the whole, not very impressing. Slow or rapid growth is by no mean diagnostic. Rapid growth need not *necessarily be caused by a malignant tu*mour Infection of the glandular tissues and ducts can very easily confuse the picture

On the other hand, slow growth does not of necessity imply only a benign tumour Inspec*tion and palpation are important.* A pharyngeal extension of the gland could be inspected in the tonsillar region. Colour changes are seen in haemangiomata. Note if the surface is smooth tuberous, fluctuating, hard, etc. Pain *need not point towards malignancy* A benign tumour located in the deep part can sometimes give a painful mastoid process.

In our experience, *facial paralysis* is seen only on very rare occasions, except in far advanced cases. It should be remembered that a malignant growth can circumvent a nerve branch without causing nerve symptoms.

Sometimes a tumour in the deep portion of the gland can increase to such an extent that the superficial part is greatly compressed, and the tumour is falsely considered to be superficial Such a tumour will displace the facial nerve laterally stretch it and produce an abnormally ascending trunk which can easily become injured if the true situation is not realised On the whole, *we should like to stress* as most important the clinical investigation In our clinic, we are of the opinion that a suspicious

lump or a probable tumour in this region should always have the surgical treatment necessary for a tumour

However other methods should sometimes be considered to confirm the diagnosis, if possible, and to clarify the situation. So, which are these methods? Radiography and sialography have, to us, given little help. We do not think that these methods give much information in addition to the clinical findings. Sometimes, a chronic infection can give a picture very similar to that of a tumour

We have not used *scintigraphy* for tumour diagnosis, but this method obviously provides a possibility of disclosing the function of the gland.

Aspiration biopsy is much favoured in some places, especially in Sweden. In Norway the pathologists have been more reluctant, partly because they feel that the cytological diagnosis is far less decisive than with the whole specimen, and partly because they fear possible growth from tumour cells lost during aspiration. This last objection does not seem to be valid, and further information of aspiration biopsy will no doubt come forth later in the discussion.

We do *not* do a regular biopsy pre-operatively Obviously there are too many risks associated with the opening of such a tumour We sometimes use a freeze biopsy but, on the whole, we prefer ordinary pathological examination of the specimen, followed a few days later by radical surgery if the postoperative pathology demands it. The opportunity then exists also to inform the patient of possible disfiguring results. We do not think it justified to damage the facial nerve without the patient's knowledge of this necessity An anastomosis, or transplantation, can be done to minimize the defect, but we, at least, cannot guarantee the result, particularly if we think that postoperative roentgen treatment is necessary

However careful the clinical evaluation and the additional investigations are, difficulties may arise as the following case history shows.

A woman, 60 years old, had for many years had chronic parotitis with numerous exacerbations. She was admitted to our department because she had, for few weeks, had a new painful swelling of her parotids. The skin over the sore swelling was inflamed, and purulent secretion was seen from the *orifice of the duct of Steno.*

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Table 3 *Diagnoses in 100 cases of parotidectomy*

Pleomorphic adenoma	70	Squamous-cell carcinoma	2
Adenolymphoma		Muco-epidermoid carcinoma	2
Cystadenofibroma	1	Undifferentiated carcinoma	1
Warthin s tumour	8	Cylindroma	4
Dermoid cysts	1	Adenocarcinoma	1
Cysts	3	Leiomyosarcoma	1
Lymphogranuloma venerum	1	Reticulosarcoma	2
Chronic parotitis	8		

In the University Clinic of Otolaryngology Ullevål Hospital, we serve about half a million people and we perform parotidectomy in about 25 cases annually In addition, a small number of other salivary-gland tumours are treated surgically

Table 3 gives a survey of 100 cases of parotidectomy performed consecutively

The numbers in the various categories are very much like those given by Eneroth

We think it is of major importance that patients with salivary-gland tumours are treated in hospitals and departments that are adequately equipped for specialized investigations have the necessary surgical experience and not least, have an excellent pathological service.

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DISCUSSION

C M Eneroth Concerning the classification of salivary-gland tumours Professor Leegaard referred to my work on parotid tumours of 1964 We still use this classification at Karolinska Sjukhuset but with some modifications based upon our studies of salivary-gland tumours in locations other than the parotid gland Especially among the intra-oral salivary glands there is, however a large group of adenomata of other types than the pleomorphic (mixed tumour) oxyphilic (oncocytoma) and papillary cyst-adenolymphoma which are not included in the original classification. Since 1966, I have worked for the WHO Cancer Unit as Head of a Collaborating Centre for Salivary-Gland Tumours The primary task is to standardize a nomenclature and to test a proposed classification by exchanging material (paraffin blocks, histological slides and diagnosis and clinical information) with other Collaborating Centres. The large group of adenomata of types other than pleomorphic and adenolymphoma has been proposed to be classified in two main groups one according to cellular pattern in trabecular tubular alveolar and cystic adenoma and the other according to cell features in oxyphilic, mucous, myo-epithelial and basal cell adenoma. Furthermore, it may be questioned whether acinic-cell adenoid cystic and papillary adenocarcinomata can be sepa-

rated as muco-epidermoid carcinoma in a low-grade and a high-grade malignant type of tumour Perhaps it may even be possible to separate a benign type of acinic-cell and muco-epidermoid tumour However there is still difficulties in making a uniform histological distinction between the well and poorly differentiated muco-epidermoid tumours.

If these and perhaps even other problems concerning salivary-gland tumours are solved, the present classification will have to be still more modified.

J Zajicek. The possibility of risk of tumour dissemination by aspiration biopsy is an important issue. No matter how fine the needles used for aspiration biopsy are, the procedure will inevitably produce microtrauma in its passage through the tissue, with consequent risk of tumour spread locally through the needle track or distally through punctured blood or lymph vessels. The risk of local tumour dissemination due to aspiration biopsy was investigated in pleomorphic adenomata (mixed tumours) which, because they are encapsulated, are well suited for such a study Follow-up of 141 patients for at least five years after aspiration biopsy has shown no local recurrence after surgical removal of benign mixed tumours (Eneroth & Zajicek, 1966)

The possibility of distal dissemination through blood or lymph vessels, with its unfavourable implications for prognosis has been carefully investigated by a research group at the Memorial Hospital for Cancer and Allied Diseases in New York (Robbins *et al* 1954 Berg & Robbins, 1962) They registered the survival times in 1406 cases of mammary carcinoma that were subjected to radical surgery and compared the survival rates of those with and without aspiration biopsy respectively The two groups did not differ as regards 10-year survival rates. The writers therefore concluded that aspiration biopsy is not detrimental to the patient and that "clinically no reason can be found not to use aspiration biopsy when it is indicated" (Berg & Robbins, 1962)

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E. Mylius It must be emphasized that recurrence or pure adenomata have never been demonstrated, while pleomorphic adenomata have a frequency of recurrence of 25 % In my opinion, there is still every reason to maintain the concept of semi-malignancy

T Leegaard (Reply to Mylius) I would like to say that the tendency to recurrency depends on the radicality of the removal of the pleomorph tumour These tumours have a very poor capsule, with part of the tumour sticking out in the surrounding gland.

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Pleomorphic adenoma	70	Squamous-cell carcinoma	4
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Table 2. *Histological classification of 349 benign and semi-malignant tumours of the parotid gland*

Benign and semi-malignant tumours	No.	%
Mixed salivary gland tumour	258	54.0
Adenoma	25	5.2
Adenolymphoma	23	4.8
Cysts	13	2.7
Haemangioma	11	2.3
Lymphangioma	6	1.3
Haemangio-endothelioma	5	1.0
Lipoma	2	0.4
Miscellaneous (neurinoma, leiomyoma, fibroma, etc.)	6	1.3
	349	73.0

various series (Rawson *et al.*, 1950 Eneroth, 1964 Eneroth *et al.* 1968 and others). While invasive destructive growth is generally accepted as a criterion of malignancy other histological features, such as high cellularity predominance of epithelial components, capsular infiltration, cylindromatous structures, incomplete encapsulation and multiple neoplastic foci are still controversial questions. As a result of this confusion, the concept of semi-malignancy has been applied to this type of tumour (Masson, 1924 Ahlbom, 1935 Rauch, 1959) However the designation semi-malignancy has, on a histological basis, in recent years been replaced by the term "pleomorphic adenoma From a clinical point of view the concept of semi-malignancy is still of practical value, based on the tendency to recurrent growth of these tumours (Mylius, 1960) The tendency to recurrence is particularly high as compared with the monomorphic adenoma. This discrepancy is in some cases partly ascribed to multiple foci of the mixed tumours. More often it is supposed to be caused by excrescences of the marginal aspect of the tumour being left behind at the first operation. However the high incidence of recurrence is mainly ascribed to the potency of the tumour cells to proliferate in the maternal tissue following contamination of this by rupture of the capsule In this way tumour metastases from implantations may develop and may later present themselves as small tumours scattered in the previous operation area. The tendency to implanting growth of pleomorphic adenomata appears to exceed the implanting power of definite malignant tumours, and it far exceeds the implanting ability of monomorphic adenomata.

In 25 patients *monomorphic adenoma* was found (5.2 per cent of the total series). In recent years, some authors have classified these tumours with mixed tumours under the common designation of pleomorphic adenoma (Willis, 1960). When pleomorphic structures in the stroma are missing, we prefer the conventional denotation of adenoma because it represents a clinically and histologically well-defined entity This group comprises only primary tumours, which means that they were not operated upon previously Metastases caused by implantation were not recorded, even in cases of unsuccessful surgery in which tumour remnants had been left behind.

One tumour was classified as *onchocytoma* and another as *acinic-cell adenoma*. Both were histologically well-defined, but the acinic-cell adenoma was difficult to differentiate from the malignant type.

Adenolymphoma or papillary cystadenolymphoma (Warthin s tumour) was revealed in 23 cases (4 8 per cent of the total series).

Table 3 *Histological classification of 77 malignant tumours of the parotid gland*

Malignant tumours	No.	%
Adenocarcinoma	15	3 1
Muco-epidermoid carcinoma	13	2.7
Cylindroma (adenoid cystic carcinoma)	12	2.6
Undifferentiated carcinoma	1	2.6
Squamous-cell carcinoma	7	1 4
Malignant mixed tumour	5	1 0
Acinic-cell carcinoma	3	0 6
Miscellaneous (Lympho-epithelioma, malignant, melanoma and lymphoma, metastases)	10	2.0
Total	77	16.0

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PAROTID TUMOURS

CLINICAL AND HISTOLOGICAL ASPECTS

P Berdal H E. Grønås and E. A. Mylius

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A report is given of 479 cases of parotid tumours admitted to the Department of Otolaryngology Rikshospitalet, Oslo. Mixed salivary gland tumours were present in 54 per cent. Benign tumours of other types (e g adenoma, adenolymphoma, angioma, cysts) constituted 22 per cent. *Malignant tumours*, comprising adenocarcinoma, muco-epidermoid carcinoma, cylindroma, undifferentiated—and squamous-cell carcinoma, malignant mixed tumour acinic-cell carcinoma, malignant melanoma and non-epithelial tumours, were diagnosed in 16 per cent. In 4.5 per cent of the cases the tumour appeared to be a non-neoplastic process. In the *majority of cases, surgical* removal of the tumour was performed In some malignant cases, supplementary X ray treatment was given. The tendency of recurrence of the mixed salivary gland tumours after unsuccessful surgery is stressed.

During the period 1952 to 1968 a total of 479 patients with a clinical diagnosis of tumour of the parotid gland were admitted to the ENT department of Rikshospitalet, Oslo Surgical removal of the tumours including resection of the parotid gland or parotidectomy was per formed in 434 cases. In 28 cases, the histologi cal diagnosis was based on minor excisions.

Table 1 *Survey of 479 tumours and pseudo-tumours of the parotid gland*

	No	%
Benign and semi-mal gnant tumours	349	73 0
Malignant tumours	77	16.0
Benign hyperplasias	14	3 0
Chronic inflammatory disorders (specific/unspecific)	22	4.5
Not classified (no operation)	17	3.5
Total	479	100.0

A survey of the series is given in Table I The definite neoplastic cases are divided into two main groups. Group I benign and semi-malignant tumours, 349 cases (73 per cent) Group II malignant tumours, 77 cases (16 per cent) A third group *denoted as benign* hyperplasias consists of obscure diseases, such *as adenolymphoid hyperplasias* (benign lymphoepithelial lesion) and lipomatosis. Chronic inflammatory disorders were found in 22 cases (4.5 per cent) comprising tuberculomata. sarcoidosis, actinomycosis and chronic unspe cific inflammations. In 17 cases, the patients were not subjected to operation.

Benign and Semi-malignant Tumours

Mixed salivary gland tumours, syn. pleomor phic adenomata, are the most frequent tu mours of the parotid gland and constitutes 54 per cent of all tumours in this series (Table 2) Two thirds of the patients were women. Forty-two patients (17 per cent) out of 258 had re-current tumours, and nine of these had been operated upon repeatedly *Information* about previous operations was lacking in some cases, but the predominant surgical procedure was enucleation of the tumours, involving a risk of capsular rupture and of leaving tumour remnants behind.

Opinions concerning the malignancy of the mixed tumours still differ owing to their complex histological features and variable clinical course. Malignant mixed tumours are compa ratively rare, ranging from 2 to 10 per cent in

Table 5 Occurrence of facial palsy in cases of malignant tumours of the parotid gland related to death by tumour

Diagnosis	No.	Facial palsy	Died of tumour with palsy
Undifferentiated carcinoma	12	8 (66 %)	5 (5)
Cylindroma	12	3 (25 %)	3 (6)
Muco-epidermoid carcinoma	13	2 (15 %)	1 (2)
Malignant mixed tumour	5	2 (40 %)	2 (3)
Adenocarcinoma	15	1 (7 %)	1 (6)
	57	16 (28 %)	12 (22)
Squamous-cell carcinoma	7	0	(6)
Acinic-cell carcinoma	3	0	(0)
Miscellaneous	10	0	(4)
Total	77	16	12 (32)

as *squamous-cell carcinoma*. The tumour was highly malignant in all cases. Five patients died of the tumour within 1–2 years. In all five the tumour infiltration was extensive. On admission to the hospital, several patients had local infiltration and metastases of such an extent that curative treatment was considered futile.

Malignant mixed tumours with invasive destructive growth into surrounding tissue were found in five cases. The infiltration was predominated by the epithelial component. It was not possible to state whether these tumours represented primary malignant mixed tumours. In view of the fact that each of the five patients had had symptoms for about 20 years, it is reasonable to assume a secondary malignancy In two cases, the tumour recurred after previous extirpation. In another case, X ray treatment had been given, and in two patients no previous treatment had been given.

The histological characteristics of *acinic-cell* carcinoma were found in three cases. Two of them are asymptomatic after 1–2 years observation. Local recurrence was seen in one case. This patient died of intercurrent disease 16 years after surgical removal of the tumour

The group *miscellaneous* includes one lymphoepithelioma, two malignant melanomata, three malignant lymphotomata and four metastatic tumours.

Involvement of the facial nerve by malignant tumours of the parotid gland usually suggests a poor prognosis. In the present series, facial nerve palsy was found in 16 patients, (Table 5) Twelve of these died of the tumour within 5 years, a mortality of 75 per cent, in contrast to 30 per cent for a corresponding group without facial palsy The incidence of facial-nerve involvement was most frequent in patients with undifferentiated carcinomata and malignant mixed tumours.

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Bilateral localisation was found in two patients. In one case the tumour disappeared gradually after biopsy and in another the tumour recurred after extirpation preceded by X ray treatment In one case the operation revealed macroscopic infiltration of tumour tissue throughout the gland, and histological examination showed multiple foci of lympho-epithelial tissue which could not be distinguished from the surrounding salivary gland tissue

Malignant Tumours

Malignant tumours were present in 77 cases (16 per cent of the total series (Table 3) *Adenocarcinomata* constituted the greatest group among the malignant tumours, viz. 15 cases. Three of the tumours were of the cystopapillomatous type The clinical course was highly malignant (Table 4) Two thirds of the patients died of tumour within 1–2 years. Most of the patients were treated by *surgery (parotidectomy)* supplemented by pre-operative or post operative X ray treatment.

Muco-epidermoid carcinoma was found in 13 cases. Histologically all of these revealed malignant characteristics with epithelial infiltration into the surrounding salivary gland tissue Clinically the malignancy was moderate. Only two patients died within 1–2 years of observation

In 12 cases the tumour showed the histological characteristics of *cylindroma* or adenoid cystic carcinoma Half of these patients died of the tumour within a five year period. Although these tumours are definitely malignant, it is often difficult to get sufficient information of their clinical course, because most of them have persisted for many years before the patients are admitted to hospital Thus, two patients who died of cylindroma had survived for 13 and 14 years, respectively after the diagnosis was confirmed histologically

Of the 12 patients with *undifferentiated carcinoma*, one third died of the tumour within 1–2 years. In spite of this gloomy outlook, five patients were free from symptoms for more than 5 years after the primary operation.

In seven cases, the tumour was classified

Table 4 *Malignant tumours of the parotid gland*
Correlation between histological types and clinical course

		Length of follow-up								
		1– years			3–4 years			≥ 5 years		
Diagnosis	No. of cases	Asymp-to-matic	Recurrence and/or met.	Died of tumour	Asymp-to-matic	Recurrence and/or met.	Died of tumour	Asymp-to-matic	Recurrence and/or met.	Died of tumour
Malignant mixed tumour	5			1			2	2		
Acinic-cell adenocarcinoma	3	1						2 (1 †)		
Adenocarcinoma	15			5	3		1	4		
Muco-epidermoid carcinoma	13	1	1	2		1		8		
Squamous-cell carcinoma	7	1		5			1			
Undifferentiated carcinoma	12		1 (1 †)	4				5 (1 †)	1	1
Cylindroma	1	2		[illegible]	3					3
Miscellaneous	10	3	(1 †)	4	1					
Total	77	1	4 (2 †)	22	7	1	6	3 (†)	1	4

† = died of intercurrent disease

Table 1 *Histological classification.*

Mixed salivary gland tumour	14
Muco-epidermoid carcinoma	2
Acinic-cell carcinoma	1
Infiltrating haemangioma	1
Angiofibroma	1
Neurinoma	1
Thyroid carcinoma, metastasis	1

Histologically 14 cases showed tumours of the mixed salivary gland type two cases were muco-epidermoid, and the remaining cases were acinic-cell carcinoma, infiltrating haemangioma, angiofibroma, neurinoma, and a metastasis from a thyroid carcinoma (Table 1).

The clinical problems associated with these tumours are primarily diagnosis and treatment. The diagnosis should not be too difficult, but experience shows that they are easily mistaken for tonsillary tumours. A superficial excision for biopsy may then lead to wrong conclusions. Puncture biopsy and a cytological diagnosis should preferably be made in such cases.

The treatment is mainly surgical. Patey and Thackray recommended division of the stylomandibular ligament to free the parapharyngeal part of the gland. In this connection, the styloid process must also be fractured in order to complete the operation by the external route. This was also recommended by Fluur in 1964

Our methods have been somewhat different, partly adjusted during the operation when confirming the size of the tumour and the ease or difficulty in dissecting it free. In 10 of the patients, the tumour was removed by a combined transoral and external dissection. In five cases, the tumour was removed transorally and in five cases externally One patient was not subjected to operation because of advanced age (83 years)

To achieve sufficient space for a safe approach to the tumour we have since 1957 cut the mandible just in front of the angulus (Fig. 3). After removal of the tumour the mandible is sutured with a stainless steel wire and allowed to heal per primam. The temporary cutting of the mandible does not complicate the surgery very much, and it offers to the



Fig. 2. Parapharyngeal protrusion of a dumb-bell tumour

surgeon possibilities of an easy dissection of the tumour from its surroundings and for ensuring the integrity of the tumour We have applied this method in six cases (Berdal, 1965) The procedure does not involve any great inconvenience on the part of the patient. A still higher degree of safety is perhaps achieved by cutting the mandible in the midline. Both the transoral and the combined transoral/external approach involve the risk of postoperative oedema with obstruction of the airway To secure an open airway it was necessary to perform tracheotomy in eight cases, which, in our opinion, should be done in all cases.

Rupture of the capsule of the tumour occurred in six cases of mixed salivary gland tumours. The calamity leads to contamination of the operative field, involving the risk of recurrence from implanted tumour cells. In these cases, a thorough irrigation of the area with saline was performed. This procedure may reduce the danger of implantation. Follow-up

Acta Otolaryng. 263 164–166 1970

PARAPHARYNGEAL GROWTH OF PAROTID TUMOURS

P Berdal and J G Hall

From the Department of Otorhinolaryngology Rikshospitalet Oslo Norway

A total of 479 patients with tumours of the parotid gland were admitted to the Department of Otolaryngology Rikshospitalet, Oslo. Of the tumours, 21 were of the dumb-bell type, showing parapharyngeal growth. Diagnosis and operative procedures are discussed. For surgical removal a transmandibular approach is recommended.

Most parotid tumours are found superficially to the facial nerve Among the more profound ly situated tumours, a parapharyngeal extension and protuberance develop in some cases. The anatomical and topographical back ground for this development of some of the parotid tumours was shown by Patey & Thackray (1957) and by Fluur (1964) (Fig. 1) A canal called the "stylo-mandibular tunnel" is formed by the base of the skull cranially the ramus ascendence of the lower jaw and the *internal pterygoid muscle ventrally and the* styloid process and the stylo-mandibular ligament dorsally *The deeper part of the parotid* gland may grow inwards into this canal in a parapharyngeal direction. This probably happens because the gland laterally is surrounded by a firm fibrous capsule, while the part extending towards the stylo-mandibular tunnel is covered by a thin fascia which allows an easier growth and extension along this route. The narrow stylo-mandibular tunnel is fixing and drawing the tumour together at this point, giving *it a hour-glass appearance, which is the origin* of the name "dumb-bell tumour"

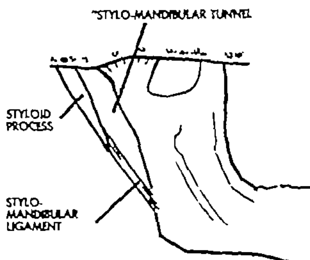


Fig. 1 Stylo-mandibular tunnel (after Fluur 19

The lateral part of the tumour may be seen and palpated from the outside, while the medial part is seen as a protrusion in the lateral part of the fauces, where the tonsil and the palatal arches are displaced medially

Among a total of 481 cases of tumour of the parotid gland admitted to the ENT Department of Rikshospitalet, Oslo 21 tumours of the dumb-bell type were found Fifteen of *these could be seen both parapharyngeally* and in the retromandibular fossa. In six cases, the *tumour was only seen parapharyngeally* (Fig. 2) Eleven of the patients had noticed a swelling of the throat or difficulty in swallowing. Another four patients had pain or an uneasy feeling in the throat six had a feeling of stuffing in the ears or were hard of hearing

The duration of the disease from the onset *of the first symptoms until operation* was less than 12 months in 14 cases In four it was between 4 and 5 years in two between 8 and 10 years, and the last patient represented a recurrence after an operation performed 23

Table 1 *Histological classification.*

Mixed salivary gland tumour	14
Muco-epidermoid carcinoma	2
Acinic-cell carcinoma	1
Infiltrating haemangioma	1
Angiofibroma	1
Neurinoma	1
Thyroid carcinoma, metastasis	1

Histologically 14 cases showed tumours of the mixed salivary gland type two cases were muco-epidermoid, and the remaining cases were acinic-cell carcinoma, infiltrating haemangioma, angiofibroma, neurinoma, and a metastasis from a thyroid carcinoma (Table 1)

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Fig. 3 The mandible, cut in front of the angulus.

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DISCUSSION

C M Eneroth In the reported series from Rikshospitalet, Oslo it is a surprisingly high frequency of parotid lesions bulging into the pharynx—21 of 481 cases. The great majority of parotid tumours (80–90 %) are localized in the superficial lobe. Of the tumours in the deep lobe, only a few attain such a size that they fill the parapharyngeal space, causing the pharyngeal wall to bulge in medially

In a study of the incidence of parapharyngeally growing parotid tumours, 1108 cases of parotid tumours operated at Karolinska Sjukhuset, were analysed Nine of them—thus less than 1 %—proved to be clinically parapharyngeal i. e a much lower frequency than in Hall's series. A remarkable fact is, however the agreement between the two series concerning the types of parapharyngeally growing parotid tumours. In Hall's case material three types were represented mixed tumour acinic cell and muco-epidermoid carcinomata and in my own from Karolinska Sjukhuset there were two types, namely mixed tumour and acinic cell carcinoma. This can be explained by the fact that the different types of tumour represented in the two series are slow-growing and usually asymptomatic on growth into the pharynx On the other hand, the highly malignant types of tumour come under treatment before they reach such a size because of their greater variety of symptoms, in the form of for example nerve infiltration and metastases.

The difference in frequency of parapharyngeally growing parotid tumours in the two series can perhaps be explained by a shorter pre-operative tumour duration in the case material from Karolinska Sjukhuset, i e the patients have come earlier to diagnosis, before the tumours have reached such a size that they bulge into the pharynx

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LIPOMATOSIS OF THE PAROTID GLAND

J Johansen and P Berdal

From the Departments of Otolaryngology and Surgical Pathology Rikshospitalet Oslo, Norway

During the period 1952–1968 a total of 462 patients with tumours of the parotid gland were subjected to operation in the Department of Otolaryngology Rikshospitalet, Oslo In three cases, histological examination revealed lipomatosis of the parotid gland associated with local subcutaneously increased fat deposits.

Case 1 A girl aged 2? years of healthy family was admitted to the department on Nov 16, 1967 for treatment of tumour of the right parotid gland. There were no remarks on pregnancy birth or neonatal period. She had been in good health with normal growth and development. In November 1966 the parents discovered swelling in front of the right ear An older sister suffered from epidemic parotitis at that time, and so the swelling was considered to be of infectious origin. As the swelling did not disappear but contrarily slowly increased in size, the patient was received in our department.

Physical examination showed firm, non-tender smooth tumour apparently invading the skin and the glandular tissue, extending from the *right* mandibular angle to the zygomatical arch. The parotid duct and the secretion seemed unaffected. No parapharyngeal involvement and no lesion of facial nerve ... was seen. The results of routine laboratory studies, including blood-cell counts and paper electrophoresis of serum proteins were normal Sialographically the tumour was seen to be closely connected laterally with the parotid gland.

After observation for 3 months in our out-patient clinic, the tumour appeared to increase in size with distinct infiltration of the skin. Subtotal parotidectomy and extirpation of the tumour were performed. The operation revealed yellowish firm tissue forming tumour-like mass with infiltration into the parotid gland and the overlying fatty tissue.

Histological examination showed a lobular glandular architecture with islands of acinic cells surrounded by numerous large fat cells. The *ductal system* seemed normal, perhaps with some proliferation of small ducts. Angiomatous proliferation was not seen (*Fig. 1*).

Case 2 A woman, aged 43 married, four children, several abortions, operatively sterilized, of healthy ancestry

The patient was admitted to the department on June 14, 1968, for surgical treatment of a tumour in the right parotid gland, rapidly developed.

Clinical examination showed 3 × 4 cm, non-tender firm, movable tumour relatively well demarcated, in the right parotid area. The parotid duct and the secretion seemed normal. There was no parapharyngeal growth, no involvement of the facial nerve.

The results of routine laboratory studies were normal. Sialography confirmed the diagnosis of tumour laterally in the parotid gland.

Operation disclosed fairly well circumscribed partially encapsulated yellowish tumour of firm consistency Histological examination revealed lipomatosis of the parotid tissue. Acinic cells formed small strains and islands between large fat cells, which appeared to have replaced most of the normal acinic cells. The ductal system seemed largely normal, perhaps with some proliferation of smaller ducts. Angiomatous proliferation was not seen (Fig. 2).

Case 3 A married woman, aged 36, one child, was admitted for operative treatment of repeated recur

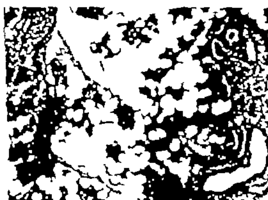


Fig. 1 Lipomatosis of the parotid gland. Numerous fat cells are seen surrounding islands and strales of acinic cells. Ducts of varying calibres (Case 1).



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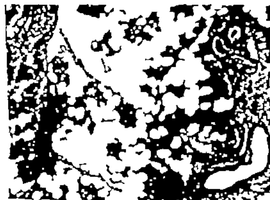


Fig. 1 Lipomatosis of the parotid gland. Numerous fat cells are seen surrounding islands and strains of acinic cells. Ducts of varying calibres (Case 1).

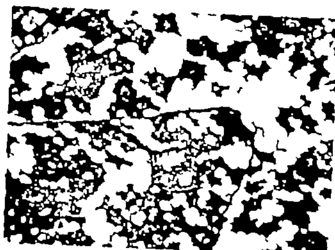


Fig 2. Lipomatosis of the parotid gland. In the lobular architecture numerous fat cells and island of acinic cells are seen. Some proliferations of small ducts(?) (Case 2).

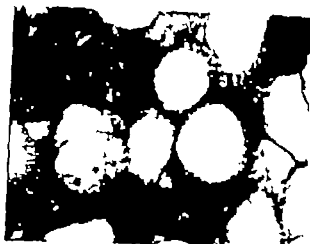


Fig. 4 Detail in cellular picture Large fat cells, degenerated acinic cells in various stages. (Case 1).

rence of a tumour of the right parotid gland on Oct 15 1967

The first appearance of the tumour was recorded in 1953 A non-tender firm, ill-defined tumour had developed within a few weeks in front of the right ear The tumour was removed in the autumn of 1953 Histological diagnosis was lipoma The tumour recurred and re-operations were performed in 1957 1958 and 1965

On admission in 1967 clinical examination showed a diffuse swelling of the right cheek involving the parotid gland The consistency of the infiltrate was partially firm, partially soft, with nodular and flat non-tender areas. Secretion from the parotid duct could not be provoked. There were no parapharyngeal growth and no marked functional facial-nerve disorders.

The result of routine laboratory studies were normal Extirpation of tumour and parotidectomy were performed. Histological examination showed atrophic glandular tissue with chronic inflammation, pronounced proliferation of small ducts and only a few pyknotic acinic cells. The main architecture of the lobular structure was preserved, with septa of dense fibrous connective tissue surrounding masses of large fat cells, ductules and inflammatory cells. No atypical cells were seen

Histochemical analysis of the tissue mainly showed triglycerides.

Lately a sixth recurrence with the same tumour like development has appeared



Fig. 3 Lipomatosis of the parotid gland. Lobular architecture Centrally ductal proliferation, single pyknotic acinic cells surrounded by several inflammatory cell and numerous fat cells (Case 3)

DISCUSSION

In these three patients, a local lipomatosis of the right parotid gland was found without relation to general adiposity Histologically it appeared to be a degenerative process in the glandular secretory epithelium with fatty transformation. This view is supported by the findings of accumulations of fat in individual acinic cells (Fig 4)

In the periglandular tissue we found an increased number of large fat cells. The aetiology of the disease is obscure Rauch (1959) gave a detailed description of sialoses, defining them as metabolic disorders related to allergic, hormonal neurovegetative disturbances and nutritional deficiency A hormonal background is mentioned by several authors (Korp, 1953 Hall, 1959) The progress in the field of lipogenetic research documenting a high potential activity of lipoid tissue might explain a rapid

transformation of the parotid gland. Empirically we know that the physiological involution of the parotid gland takes place through a lipomatous degeneration. In the other salivary glands, this process is brought about by fibrosis.

The surgical treatment of lipomatosis in our patients did not arrest the disease. In comparison, it may be mentioned that in cases of clear-cut lipomata, no recurrence was seen.

Reports on lipomatosis of the parotid gland are few and our knowledge of this disease is limited. We believe that further studies of the problem by histochemical and biochemical methods may throw light on the problems involved.

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CYLINDROMA OF SALIVARY GLANDS

A REPORT OF 80 CASES

P Berdal A de Besche and E Mylius

From the Department of Otolaryngology Rikshospitalet Oslo and the Department of Pathology Sentralsykehuset Trondheim Norway

Eighty cases of cylindroma (adenoid cystic carcinoma) from the Department of Otolaryngology Rikshospitalet Oslo are reviewed. Clinical and histological characteristics are discussed. Special attention is drawn to a tendency to involvement of nerves.

Cylindroma (Billroth 1859) synonym adenoid *cystic carcinoma (Ewing, 1928)* is a malignant epithelial tumour which develops in large and small salivary glands In Norway cylindroma is notified to the Register of Cancer and constitutes about 1 15 per thousand of all malignant tumours (within the 10-year period from 1956 to 1965 115 cases of cylindroma. Total number of new cases of cancer all types, about 100 000)

To illustrate some of the clinical features of cylindroma 80 cases from the Department of Otolaryngology Rikshospitalet Oslo are briefly mentioned below The patients were seen during the years 1952–68

Most patients were between 40 and 50 years of age when the first symptom of disease was observed No sex-difference

Localization	No. of cases
Parotid gland	14
Submandibular gland	9
Mouth/pharynx	32
Nose/sinuses/orbit	12
Larynx/trachea	10
Middle ear	3

The duration of disease is shown in Fig. 1 It shows the intervals between the onset of symptoms until the diagnosis was made, and how long the patients have been living with the disease after the diagnosis was made and therapy started Thirty three patients died of cylindroma Three patients died of cerebral haemorrhage Twenty-two are alive and without signs of recurrence after more than 5 years. Twenty two patients are alive and fairly well with recurrence and or/metastases.

Among many distinctive features of cylindroma we particularly want to point at a marked tendency of the tumour to perineural *and intraneural growth (Fig. 2) and to clinical* symptoms from sensory and motor nerves.

Before the diagnosis was established several of our patients had been treated for many years for pain in the trigeminal area In some of the cases the pain was very severe and could not be relieved by analgesics That the diagnosis was made relatively late in these cases may be ascribed partly to a macroscopically minimal neoplastic infiltration and partly to inadequate knowledge of this type of tumour Paresis of the facial nerve and hypoglossal nerve has also been present in cylindroma patients for a long time before the diagnosis was made

It appears that the cylindroma also has a tendency to perivascular and intravascular growth (Fig. 3) However the perivascular growth is not seen so frequently or is not so marked as in the perineural area The peri-

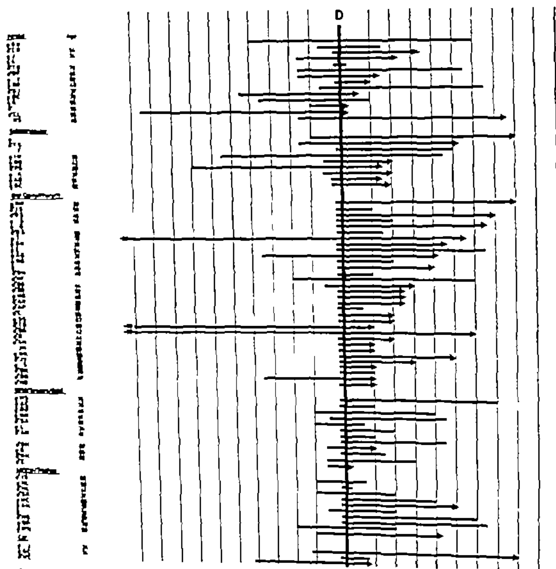


Fig 1 Duration of disease

vascular infiltration may be responsible for the development of ectatic vessels which can often be seen in the skin and mucous membrane covering the tumour

Intravascular growth of the tumour at an early stage probably explains why haematogenous metastases appear more frequently and also earlier than lymphatic metastases and may occur many years after the extirpation of the primary tumour

Histologically it is noticed that only minimal infiltration by lymphocytes and macrophages occurs. Usually there are neither necrosis nor bleeding in the tissue of the tumour These

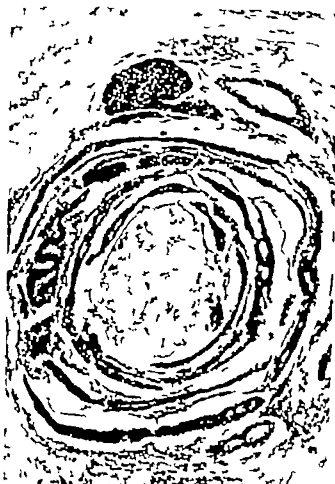


Fig. 2. Perineural growth of cylindroma



Fig 3 Perivascular growth of cylindroma.

features may to some extent, explain why cylindromata rarely ulcerate in spite of infiltration of the mucous membrane or skin

In the treatment it may be necessary in the individual patient in the long run to apply both surgery and radiological and chemotherapeutic methods

Extirpation of the tumour will, in most cases, be the principal treatment, aiming at radical removal. In spite of surgical removal which may appear to be radical a new tumour *is often seen close to or far from the original* site due to the tendency of the tumour to infiltrate long nerves and blood vessels. Electrocoagulation of the tumour may be appropriate in the trachea and bronchi

Concerning radiological treatment, it has been emphasized by many authors that the cylindroma is radioresistant. In our opinion this view is too categorical Some years ago we were of the same opinion Later we have, in many cases, seen a temporary good effect of X-ray treatment From a radiotherapeutic point of view a cylindroma may be looked upon as radiosensitive, but not radiocurable. Lack of radiocurability may to some extent be connected with its peculiar way of growth along nerves and vessels, resulting in infiltration far away from the primary tumour Thus, it may happen that the irradiation fields do not cover the entire tumour area.

Chemotherapy has been tried in a few cases. *In two cases, Vinblastin (Velbe Lilly")* probably retarded the growth of the tumour as judged from the growth or pulmonary metastases. Methyehydrazin (Natulan "Roche") seems to have a more pronounced cytostatic effect than Velbe.

Corticosteroids seem to exert a favourable influence both on the growth of tumour and *the general condition of the patient We have* used steroids in advanced cases only

The prognosis is not very good. Many patients died of their cylindroma, but we have also seen 22 cases which appear to be cured with no recurrence after 5 years or more. Of these, six have been free from recurrences for periods from 10 to 17 years. In predicting the prognosis, it should be borne in mind that the general state of health and the capacity for work may be only slightly affected for a long time, often for several years, even in patients with multiple and major pulmonary metastases. We do not know of any other malignant epithelial tumour than cylindroma, with which the patient can survive with his disease for a long time and to enjoy subjective well-being.

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DISCUSSION

C. M. Eneroth: The term "adenoid cystic carcinoma" is nowadays much more used for this type of tumour because cylindroma is a diffuse conception, indicating several independent types of tumour with cylindromatous structures, but even "adenoid cystic carcinoma" is to some degree a misleading description, as cystic structures are not typical in this type of tumour as in papillary cystadenolymphoma and muco-epidermoid carcinoma.

A series of about 1700 parotid tumours (300 malignant) treated at Karolinska Sjukhuset confirms that adenoid cystic carcinoma has a special tendency to neural invasion. Thus, peri- and intraneural growth of the tumour caus-

Table 1. *Spontaneous paralysis of the facial nerve by different types of parotid tumour (1678 cases)*

Type of tumour	Spontaneous paralysis of the facial nerve per cent
Pleomorphic adenoma	0
Papillary cystadenolymphoma	0
Oncocytoma	0
Carcinoma in pleomorphic adenoma	14
Muco-epidermoid carcinoma	8
Adenoid cystic carcinoma	29
Acinic-cell carcinoma	3
Papillary adenocarcinoma	9
Solid poorly differentiated carcinoma	24

ing spontaneous paralysis of the facial nerve occurred in 29 % of the cases with adenoid cystic carcinoma. A comparison with other types of parotid tumours appears from the table.

Spontaneous paralysis of the facial nerve proved to imply a hopeless prognosis, as all these patients died in tumour disease: all of them within 8 years of the onset of the paralysis. Adenoid cystic carcinoma is characterized by a prolonged clinical course, often with late appearance of recurrences and metastatic spread. The long-term prognosis is grave and an analysis of more than 2500 salivary gland tumours has shown that a much longer follow-up than 5 years is necessary to disclose the definite prognosis in adenoid cystic carcinoma. We have found, however, that there is a difference between adenoid cystic carcinomata, which are dominated by a cribriform component (low-grade malignant) and those which are dominated by a solid component (high-grade malignant). In rapidly growing tumours, such as solid adenoid cystic carcinoma, epidermoid carcinoma and undifferentiated carcinoma, the poor prognosis is already evident from a 5-year follow-up. A much longer follow-up is, on the other hand, necessary to disclose the definite prognosis in more slow-growing tumours, such as adenoid cystic carcinoma dominated by the cribriform component.

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INCIDENCE AND PROGNOSIS OF SALIVARY-GLAND TUMOURS AT DIFFERENT SITES

A STUDY OF PAROTID SUBMANDIBULAR AND PALATAL TUMOURS IN 2632 PATIENTS

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In a histological re-examination and re-classification of 2632 palpable lesions of the parotid submandibular and palate regions, 2311 exhibited the structures characteristic of true salivary-gland tumours. Tumours originating in the various major and minor salivary glands have essentially similar histological features. The relative incidence of the different types of true salivary gland tumours and their prognosis have been shown to vary with their location One out of six salivary gland tumours in the parotid gland, one of three in the submandibular gland and almost half of the tumours in the palate proved to be malignant. A long-term clinical follow-up study revealed a difference in prognosis for a given type of malignant salivary gland tumour at various sites. The prognosis seems best when the primary tumour is located in the palate less favourable when it is in the parotid gland, and least favourable in the submandibular gland.

Tumours originating in the various major and minor salivary glands have essentially similar histological features. The purpose of this study is to determine whether the incidence of the various types of tumour and their prognosis vary with the location.

The three most common sites of involvement for salivary gland tumours are the parotid and submandibular glands and minor salivary glands of the palate About 95 % of all salivary gland tumours are considered to be located at these sites, whereas the remaining 5 % are found in other minor salivary glands than those of the palate and in the major sublingual glands (Seifert, 1966) Although there is an extensive literature on these tumours, no large operative series treated in the same clinic has been described especially as regards the submandibular and minor salivary-gland tumours This is largely due to the fact that these tumours are relatively uncommon. As a consequence, it is very difficult to compare the incidence of various types of tumour and their prognosis in different locations

To carry out a comparative study of this kind one must have not only data concerning a large number of operated tumours in various locations, but also a meticulous long term clinical follow up study In order to compare the histological and clinical features and the prognosis of salivary-gland tumours in various locations in as many cases as possible a study of tumours was made in the three locations where most salivary-gland tumours occur i.e in the parotid and the submandibular gland and the palate region.

MATERIAL

The study is based on a histological and clinical survey of parotid, submandibular and palate tumours in 2632 patients treated in the Department of Otolaryngology and Radiumhemmet, Karolinska Sjukhuset, during the period 1909–1965 (only a few cases in the series were treated before 1925)

A histological reclassification of all tumours was made as well as a complete long-term clinical follow up study starting with the first histological verification of the tumour A rough estimate of the prognosis is obtained by the incidence of metastases and by calculation of the determinate survival rate (D S. R) during a follow-up period of 5–40 years. D S R. im

Table 1. *Reclassified tumours of the parotid gland, the submandibular gland and the palate region (2632 patients). Distribution of salivary gland tumours in these locations.*

Location	Total No. of tumours	Salivary-gland tumours	
		No.	%
Parotid gland	2067	1983	96
Submandibular gland	187	161	86
Palate	378	167	44
Total	2632	2311	

plies that the survival rate is based on determinate groups, which do not include patients lost to follow-up or those dying without signs of tumour disease. Since no patient in the follow-up series was lost, the D. S. R. is thus based on mortality in the tumour disease.

RESULTS

In each of the three locations examined, a palpable lesion consists in varying degrees of a true salivary-gland tumour. Table 1 shows that a "tumour" of the parotid and submandibular glands generally is a true salivary-gland tumour—in the parotid almost always (96 %) and in the submandibular in five cases out of six. In the palate, however, not even half of all tumours are true salivary-gland tumours.

The difference in incidence between the palate and the major salivary glands (parotid and submandibular) can to some extent be explained on histogenetical grounds. A very large proportion of "tumours" in the palate thus originate from the squamous epithelium of the mucous membrane (142 tumours). In the major salivary glands, however, there are also tumours that do not arise in the actual salivary-gland parenchyma. These include mesenchymal tumours and so-called pseudotumours, i.e. localized swellings of varying origin, such as inflammation, hyperplasia and cyst formation.

As regards the distribution of true salivary gland tumours in various locations, the incidence is strikingly high in the parotid as compared with the other locations. The fact that a salivary-gland tumour is 12 times as frequent in the parotid as in the submandibular gland is difficult to explain histogenetically. The difference cannot be based on size alone, because the two parotids weigh 40–60 g, while the two submandibular glands weigh 20–30 g (Seifert, 1966). According to Durrani (1964) this large difference between the incidence in the two glands suggests that there must be some factors at work that make the parotid more susceptible to tumours than the submandibular gland.

The distribution of various types of true salivary-gland tumours in various locations is shown in Table 2. It will be seen that true salivary-gland tumours include a large number of types. There is, however, a striking predominance of a single type of tumour—namely pleomorphic adenoma (previously termed benign mixed tumour): four out of five salivary gland tumours of the parotid gland and more than half of tumours of the submandibular gland and the palate thus fall under the heading of pleomorphic adenoma.

As regards malignant tumours of the salivary glands, there is a remarkable difference in the incidence of adenoid cystic carcinoma in the various locations: 2 %, 16 %, 22 %.

Why is the relative incidence of this type of tumour eight times higher in the submandibular gland than in the parotid gland? Can there be a histogenetical explanation? In the palate, two types of tumour strongly predominate—muco-epidermoid and adenoid cystic carcinoma. In the submandibular and, particularly, in the parotid gland the malignant salivary-gland tumours are more evenly distributed among the different types.

Differences in histology may provide an explanation of differences in incidence between various types of tumour in various locations. This is easy to understand when a comparison is made between major and minor salivary

Table 2 *Reclassified salivary gland tumours of the parotid gland the submandibular gland and the palate (2311 patients) Distribution of different types in these locations*

Type of tumour	Parotid gland	Submandibular gland	Palate
Benign			
Pleomorphic adenoma	1544 (78 %)	95 (59 %)	93 (56 %)
Papillary cystadenolymphoma	76	4	–
Oncocytoma	18	1	–
Malignant			
Carcinoma in pleomorphic adenoma	31		3
Muco-epidermoid carcinoma	80 (4 %)	6 (4 %)	27 (16 %)
Adenoid cystic carcinoma	40 (2 %)	25 (16 %)	36 (2[illegible] %)
Acinic cell carcinoma	58	1	1
Mucus-producing adenopapillary carcinoma	49	–	6
Solid undifferentiated carcinoma	80	15	1
Epidermoid carcinoma	7	11	–
Total	1983	161	167

glands A comparison between the parotid and the submandibular glands, however reveals differences not only in the acini—the parotid gland being composed entirely of serous cells, whereas the submandibular gland contains mucous cells as well as serous cells, but also a histological difference in the duct system (Rother 1963)

If the various types of true salivary-gland tumours are divided into a benign and a malignant group, it appears from Table 3 that the incidence of malignancy is lowest in the parotid gland and highest in the palate Thus, about one out of six tumours in the parotid gland one of three in the submandibular gland and almost half of the tumours in the palate are malignant It is noteworthy that the relative incidence of malignant tumours of the salivary glands is twice as high in the submandibular as in the parotid gland.

Table 3 *Reclassified salivary gland tumours of the parotid gland the submandibular gland and the palate region (2311 patients) Distribution of malignant salivary gland tumours in these locations*

Location	Total No. of salivary gland tumours	Malignant salivary gland tumours	
		No.	%
Parotid gland	1983	345	17
Submandbular gland	161	61	38
Palate	167	74	44
Total	2311	480	

Departing for a moment from true salivary gland tumours, I should here like to consider the incidence of malignancy of all tumours in the three locations, thus including not only tumours of the salivary-gland type but also "pseudotumours" and tumours that do not arise in the actual salivary gland parenchyma. It must be of interest from the clinical viewpoint to determine how great the risk is that a tumour occurring in the parotid, submandibular or palatal region will be malignant. Table 4 shows that about one out of six tumours in the parotid gland one of three in the submandibular gland and more than half of all tumours in the palate are malignant The incidence of malignancy in the total tumour and the true salivary gland tumour material, respectively is in good agreement as regards parotid and submandibular tumours (cf Tables 3 and 4) In the palate on the other hand

Table 4 *Reclassified tumours of the parotid gland the submandibular gland and the palate region (2632 patients) Distribution of malignant tumours in these locations*

Location	Total No. of tumours	Malignant tumours No.	%
Parotid gland	2067	359	17
Submandibular gland	187	62	33
Palate	378	217	57
Total	2632	638	

the risk of malignancy is greater in cases of palpable lesion than when a true salivary-gland tumour is present. To some extent this is due naturally to the large number of squamous-cell carcinomata in the palate (122 cases).

It is not known whether and to what extent the prognosis varies when the same type of malignant tumour occurs in different locations. Prognoses for various kinds of malignant tumours in various locations have been determined by a study of the incidence of metastases and the determinate survival rate (D.S.R.) over a long follow-up period.

In spite of the fact that the present series is larger than any previously reported, most of the groups of salivary-gland tumours located in the submandibular gland and the palatal region are too small to be discussed in this connection. No conclusions on the prognosis have been drawn when the tumour groups consisted of fewer than 10 cases.

The incidence of metastases of different types of tumours in different locations is shown in Table 5

X indicates those groups which are considered too small to merit discussion. Only one type of tumour i.e., adenoid cystic carcinoma occurs in sufficient numbers in all three locations to justify conclusions based on a comparison. The incidence of metastases is considerably higher when the primary tumour is located in the submandibular gland than in the parotid gland or the palate. Thus, adenoid cystic carcinoma metastases more than twice as often when located in the submandibular gland as in the palate.

It is apparent that an increased incidence of metastases is associated with a poorer prognosis. This is shown in Fig. 1 which gives the determinate survival rate (D.S.R.) for adenoid cystic carcinoma in various locations. When the primary tumour is located *in the* palate, the prognosis is best. When it is located *in the* parotid gland, the prognosis becomes worse, and in the submandibular gland worst. In other words, the prognosis is aggravated in parallel with an increased incidence of metastases (Table 5).

The incidence of metastases and consequently the prognosis of a given type of tumour are influenced by various factors, such as the drainage of lymph from the primary tumour lo-

Table 5 *Malignant salivary-gland tumours of the parotid gland the submandibular gland and the palate: Incidence of metastases during the follow-up period (X eplaces figures too small to be discussed in this connection)*

Type of tumour	Parotid gland No.	%	Submandibular gland	Palate
Carcinoma in pleomorphic adenoma	9/21	43	X	X
Muco-epidermoid carcinoma	7/63	11	X	2/26 (8 %)
Adenoid cystic carcinoma	15/35	43	15/20 (75 %)	11/32 (34 %)
Acinic cell carcinoma	7/37	19	X	X
Mucus-producing adenopapillary carcinoma	13/47	28	X	X
Solid undifferentiated carcinoma	43/75	57	X	X
Epidermoid carcinoma	X	–	X	X

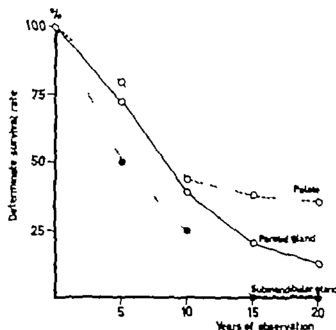


Fig. 1 Relation between duration of observation and determinate survival rate of adenoid cystic carcinoma at different sites.

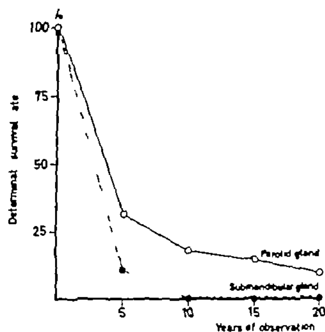


Fig. 2. Relation between duration of observation and determinate survival rate of solid undifferentiated carcinoma of the parotid and submandibular gland

cation and the pre-operative duration of symptoms The longer the interval between the onset of symptoms and the treatment of the malignant tumour the greater the risk of metastases and as a consequence the worse the prognosis. The correspondence between the pre-operative duration of the tumour increased incidence of metastases and worsening of the prognosis is clearly evident from the study of cases of adenoid cystic carcinoma in various locations, in which the pre-operative duration of symptoms averaged 1 9 years in the palate, 3 7 years in the parotid and 5 6 years in the submandibular gland.

That the prognosis is worse when a given type of tumour is located in the submandibular rather than in the parotid gland is clear from Fig. 2, which shows the D.S.R. for solid undifferentiated carcinoma after 5 10 15 and 20 years in these locations.

The results of the long-term clinical follow up study suggest that the prognosis for a given type of malignant tumour varies according to its location. Moreover the prognosis seems most favourable when the primary tumour is in the palate less favourable when it is in the parotid gland and least favourable in the submandibular gland.

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TUMOURS OF THE PALATE

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A histological reclassification of 383 tumours of the palate showed that salivary-gland tumours and epidermoid carcinomata constituted the two largest groups, with 170 and 123 cases, respectively. Of the total number 219 cases were malignant, which means that the risk of a palatal tumour being malignant is 57 %. A long-term clinical follow-up study disclosed a much better prognosis for the malignant salivary gland tumours than for the epidermoid carcinomata. In the latter group of tumours, the incidence of ulceration was much higher. The presence of ulceration in a tumour of the palate may therefore be considered to indicate an unfavourable prognosis. Salivary-gland tumours were more commonly found in the hard palate, and epidermoid carcinomata in the soft palate.

In the palate, a wide variety of tumours may develop, originating in the epithelium, the connective tissue and the minor salivary glands. Most studies of salivary-gland tumours are concerned with tumours in the major salivary glands, while those dealing with tumours in the minor salivary glands are relatively few. This situation is hardly surprising, since only about 10 % of the relatively rare salivary gland tumours are considered to originate in the minor salivary glands (Seifert, 1966). It is, therefore, difficult to collect any considerable quantity of these tumours. More than half of the intra-oral salivary-gland tumours appear in the palate (Lucas, 1964), which means that the palate is the most common location for these tumours. We have accordingly chosen the palatal tumours as the subject for a histological and clinical study. For the clinical evaluation a long-term follow-up study is of great value, particularly as only a few similar examinations covering a large number of palatal tumours have been reported.

MATERIAL

The present study is based on a analysis of all histologically verified tumours of the palate in 383 patients, registered at Radiumhemmet during the period 1919–1966. A histological re-examination was made of all the tumours, which were then reclassified according to a more differentiated nomenclature (Foote & Frazell, 1954; Eneroth, 1964). With a few exceptions, all the patients were re-examined regularly and it was therefore possible to carry out a histological and clinical correlation study. The prognosis was established by studying the determinate survival rate, which is based on determinate groups. The determinate groups do not include patients lost to follow-up and those dying of intercurrent disease.

RESULTS

In the histological reclassification, the 383 palatal tumours were distributed according to the various types shown in Table 1. Salivary-gland tumours occurred in 170 cases, i.e. 44 % of the total number of palatal tumours. They were benign in 95 and malignant in 75 cases. Squamous-cell tumours occurred in 143 cases. The 20 benign tumours in this group were all papillomata, while the 123 malignant were all epidermoid carcinomata. Thirty-three tumours

Table 1 *Distribution of 383 tumours of the palate after reclassification*

Diagnosis	No. of tumours	
Salivary gland tumour		170
Benign	95	
Malignant	75	
Squamous-cell tumour		143
Benign	0	
Malignant	143	
Mesenchymal tumour		33
Benign	20	
Malignant	13	
Malignant melanoma		8
Non-neoplastic lesion		29
Total		383

Table 3 *Distribution of 33 mesenchymal tumours of the palate after reclassification*

Diagnosis	No. of tumours	
Benign		20
Polypoid fibroma or angiofibroma	14	
Haemangioma	2	
Angioleiomyoma	2	
Angioblastoma	1	
Fibrolipoma	1	
Malignant		13
Neurofibrosarcoma	3	
Angiosarcoma		
Osteosarcoma	1	
Malignant lymphoma	7	
Total		33

were mesenchymal 20 being benign and 13 malignant. The series included eight cases of malignant melanoma, a type of tumour which very rarely occurs in the oral cavity According to the Swedish Cancer Register there were only four diagnosed cases of malignant melanoma in the oral cavity during the 5 year period 1958–1962 All the tumours in the present study were clinically considered to be neoplasms prior to the histological examination However 29 cases turned out to be due to a non-neoplastic disease, i e. a localized mass of varying nature for example, hyperplasia or granuloma.

The distribution according to the type of salivary gland tumour is shown in Table 2. All of the 95 benign salivary gland tumours were pleomorphic adenomata and they constituted 56 % of the total number of salivary-gland tumours. In a strikingly large proportion of the pleomorphic adenomata, the structure was so uniformly epithelial that the tumours could be classified as monomorphic adenomata. Malignant salivary-gland tumours occurred in 75 cases, and the two preponderant types of tumour were muco-epidermoid carcinoma and adenoid cystic carcinoma, with 27 and 37 cases, respectively Together these two types accounted for 85 % of all the malignant salivary gland tumours of the palate. The other malignant tumours of the salivary glands, acinic cell carcinoma mucus-producing adenopapillary carcinoma, solid undifferentiated carcinoma and carcinoma in pleomorphic adenoma constituted altogether only 11 cases.

Table 2 *Distribution of 170 salivary-gland tumours of the palate after reclassification*

Diagnosis	No. of tumours	
Benign		95 (56 %)
Pleomorphic adenoma	95	
Malignant		75 (44 %)
Muco-epidermoid carcinoma	27	
Adenoid cystic carcinoma	37	
Acinic-cell carcinoma	1	
Mucus-producing adenopapillary carcinoma	6	
Solid undifferentiated carcinoma	1	
Carcinoma in pleomorphic adenoma	3	
Total		170

Table 3 shows the distribution of the mesenchymal tumours Of the 20 benign tumours, 14 were polypoid fibroma or angiofibroma, and of the 13 malignant seven were malignant lymphoma. Other types of mesenchymal tumours occurred only in isolated cases.

The incidence of malignant tumours of the palate varies considerably in different series. Thus, according to Dahlin (1968) it was 34 % and according to Boyle & Cole (1968) 75 % In the present study there was a 57 % risk

Table 4 *Follow-up study of malignant salivary gland tumours and epidermoid carcinomata of the palate*

	Determinate survival rate, %	
Observation period (years)	Malignant salivary-gland tumour	Epidermoid carcinoma
5	77	41
10	61	30
15	55	22
20	50	13

that a tumour of the palate was malignant. The two principal groups of malignant tumours are the malignant salivary-gland tumours and the epidermoid carcinomata, which together make up 90 % of all malignant tumours of the palate. These two groups reveal a definite difference in prognosis, as shown in Table 4. As regards the malignant salivary-gland tumours the determinate survival rate drops from 77 % in the 5-year group to 50 % in the 20-year group. The corresponding figures for epidermoid carcinomata are 41 % and 13 % respectively. The prognosis is thus poorer for epidermoid carcinomata.

Is there any clinical evidence of malignancy when a neoplastic change is found in the palate? A pigmented, easily bleeding, ulcerated tumour of the palate should give a strong suspicion of a highly malignant tumour. In all eight cases of malignant melanoma in the present study the tumour had these characteristics, and all these patients died of the tumour disease within 5 years.

Table 5 shows that there is a definite difference in the incidence of ulceration between different groups of malignant tumours of the palate. Ulceration was present in 22 of 75 malignant salivary-gland tumours (29 %) and in 90 of 123 epidermoid carcinomata (73 %). The prognosis in epidermoid carcinoma was considerably worse than in the malignant salivary gland tumours. Ulceration of a tumour of the palate can therefore be considered to indicate an unfavourable prognosis in view of the much higher incidence of ulceration in epidermoid carcinoma than in malignant salivary-gland tumours.

The localization in the palate of the two largest groups of tumours, i. e., the salivary-gland tumours and the epidermoid carcinomata, is shown in Table 6. Of the 170 salivary

Table 5 *Frequency of ulceration in malignant salivary-gland tumours and epidermoid carcinomata of the palate*

Diagnosis	Total No. of cases	Ulceration No. of cases
Malignant salivary-gland tumour	75	22 (29 %)
Epidermoid carcinoma	123	90 (73 %)

Table 6. *Location in the palate of salivary-gland tumours and epidermoid carcinomata.*

	Salivary-gland tumour			Epidermoid carcinoma
Location	Benign No. of cases	Malignant No. of cases	Total No. of cases	No. of cases
Hard palate	60	54	114 (67 %)	48 (39 %)
Soft palate	29	15	44 (26 %)	59 (48 %)
Hard and soft palate	6	6	12	16
Total	95	75	170	123

gland tumours, 114 (67 %) were situated in the hard palate while only 48 (39 %) of the 123 epidermoid carcinomata were found in this region A difference as regards the localization to the hard or soft palate has accordingly been demonstrated to exist in these two different groups of tumours. The salivary gland tumours were most common in the hard palate while the epidermoid carcinomata were more frequently observed in the soft palate which is in accordance with the observations of Martin (1942)

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CYTOLOGICAL DIAGNOSIS OF SALIVARY-GLAND CARCINOMATA FROM ASPIRATION BIOPSY SMEARS

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In 100 consecutive cases of salivary-gland carcinoma in which aspiration biopsy had been performed before operation, the cytological findings were compared with the histological diagnoses. Morphological features are described which should prove useful in the differentiation between various types of salivary-gland carcinoma in smears of aspirate—adenoid cystic, acinic cell, mucus-producing adenopapillary trabecular adenocarcinoma, muco-epidermoid carcinoma and undifferentiated carcinoma.

Malignant epithelial tumours of the salivary glands are commonly classified according to their morphological characteristics in tissue sections as adenocarcinoma of various types, muco-epidermoid carcinoma and undifferentiated carcinoma (Foote & Frazell, 1954 Eneroth, 1964) Studies of the long-term survival rates after treatment for these tumours indicate that the clinical course is dependent on the histological type (Eneroth *et al.*, 1966, 1967 Blanck *et al.* 1967). It may therefore be expected that the treatment of malignant salivary-gland tumours, i. e. the extent of surgery and whether or not pre-operative irradiation is to be given, will increasingly be determined by the type of the neoplasm, which consequently must be known to the clinician.

Aspiration biopsy of salivary-gland tumours with a fine needle (22 gauge) yields material for cytological analysis. Benign neoplasms in these sites, such as oncocytic tumours (papillary cystadenoma lymphomatosum and oncocytoma) and mixed tumours can in most cases be recognized from a study of aspiration biopsy smears (Eneroth & Zajicek, 1965, 1966). The present paper is concerned with the morphology of cells in aspirates from carcinomata of the salivary glands. The cytological slides from 100 such tumours were reviewed. The morphological details which permit identification of the tumours pre-operatively by fine-needle aspiration biopsy are described.

MATERIAL

The 100 tumours were consecutively investigated primary carcinomata of the salivary glands. The diagnosis was histologically established in all cases. The histological types were as follows: adenoid cystic, 31 cases, acinic-cell, 28 mucus-producing adenopapillary 5 trabecular adenocarcinoma, 1 muco-epidermoid carcinoma, 20 and undifferentiated carcinoma, 15 cases (six arising in pleomorphic adenoma).

RESULTS AND CONCLUSIONS

Adenoid cystic carcinoma. The initial cytological reports in the 31 cases of histologically verified adenoid cystic carcinoma are presented in table 1 in which the cases are grouped according to the period during which the aspiration biopsy was performed, viz. 1953–1965 or 1966–1967 Contrary to what might have been expected in adenocarcinomata of "cystic" type, the cytological report stated "cyst" in only one of the 31 cases. "Cystic" is therefore a somewhat misleading description. Abundant neoplastic material was obtained in the other 30 cases. In 14 of them, pleomorphic adenoma (mixed tumour) was reported—13 from 1953–

Table 1 *Initial cytological reports from aspiration biopsy in 31 histologically verified primary adenoid cystic carcinomata*

Initial cytological diagnosis	Time of cytological diagnosis	
	1953–1965	1966–1967
Cyst	1	–
Pleomorphic adenoma	13	1
Carcinoma	8	–
Adenoid cystic carcinoma	–	8
Total	2.	9

1965 and one in 1966 Carcinoma was cytologically reported in eight cases, all from the first period and the cytological diagnosis was adenoid cystic carcinoma in eight cases, all from 1966–1967

The cells aspirated from the adenoid cystic carcinomata had round or oval nuclei surrounded by a scarcely detectable rim of cytoplasm (Fig. 1 A) Cell size showed little variation. In addition to tumour cells, cylindrical structures —globules of mucus—were seen in the slides from 18 of the 31 adenoid cystic carcinomata (Fig. 1 A) Such globules were not seen in aspirates from the other salivary-gland tumours, including the pleomorphic adenomata. Their presence may therefore be regarded as indicative of adenoid cystic carcinoma (Eneroth & Zajicek, 1969) This is important when the cytologist is otherwise in doubt as to whether he is dealing with a pleomorphic adenoma (mixed tumour) or a carcinoma. Recognition of malignancy will in such cases be based partly on the cells, but mainly on their mucinous product with its characteristic globules.

The presence of mucus globules suggests that the adenoid cystic carcinoma is of highly differentiated type (Eneroth *et al* 1967) The predominantly solid, poorly differentiated adenoid cystic carcinomata in this study did not yield such distinct "cystic" (mucoid) aspirate

In adenoid c ys c carcinoma of low differentiation the rec nition of malignancy is not difficult, but ytological typing of the tumour is not always possible. In such cases, the cytologist can only report a carcinoma and the typing must await histological analysis, which may disclose predominantly solid adenoid cystic carcinoma.

Acinic-cell carcinoma. Table 2 shows the initial cytological reports in the 28 cases of acinic-cell carcinoma. Here too, the tumours are grouped according to the time of diagnosis. Benign epithelial tumour usually adenoma, was cytologically reported in 12 cases, 10 of them from the period 1953–1962 and two from 1963–1967 Carcinoma was cytologically suspected in two cases from the first period. Carcinoma without further specification was reported in three cases. Acinic-cell carcinoma was suggested or diagnosed in 11 cases, seven of them from the second period of the study The review of the slides showed that the smears from acinic-cell carcinomata characteristically contained clusters of cells with central nuclei and abundant foamy cytoplasm. Generally no clear-cut cellular atypia was seen, and the diagnosis was based on the presence of numerous acinic cells in solid plugs with total absence of ductal epithelium (Fig 1 B)

Other adenocarcinomata. From the five mucus-producing adenopapillary adenocarcinomata and the single trabecular adenocarcinoma, abundant tumour material was obtained The aspirate consisted partly of plugs of overlapping cells and partly of sheets of cells in more regular arrangement. The individual cells in

Table 2 *Initial cytological reports from aspiration biopsy in 28 histologically verified primary acinic-cell carcinomata*

Initial cytological diagnosis	Time of cytological diagnosis	
	1953–1962	1963–1967
Benign epithelial tumour	10	
Suspectedly malignant epithelial tumour	2	–
Carcinoma, type unspecified		1
Acinic-cell carcinoma	4	7
Total	18	10

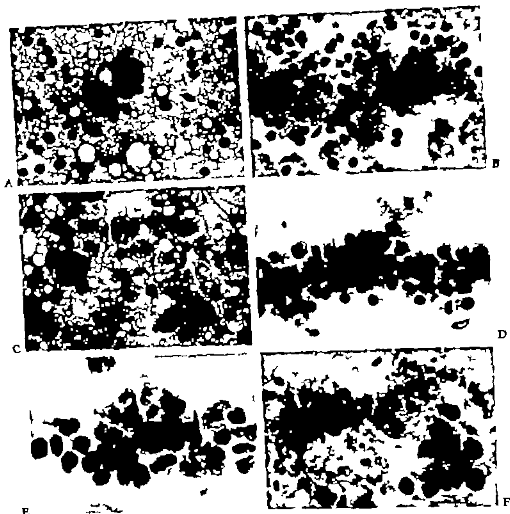


Fig. 1 A–F

Aspiration-biopsy smear from:

A. Adenoid cystic carcinoma showing two pink stained globules of mucus surrounded by carcinoma cells.

B. Acinic-cell adenocarcinoma. A cluster of carcinoma cells exhibiting round nuclei and somewhat foamy cytoplasm is shown.

C. Adenopapillary mucus-producing adenocarcinoma. Carcinoma cells exhibit round nuclei surrounded by large amount of cytoplasm. In one of the cells globule of mucus-like material is seen.

D Muco-epidermoid carcinoma of low malignancy A cluster of carcinoma cells with moderate nuclear atypia is shown.

E. Low-differentiated carcinoma. Pronounced nuclear atypia with decreased nuclear/cytoplasmic ratio is seen.

F Low-differentiated carcinoma arisen in pleomorphic adenoma. A plug of polymorphic carcinoma cells is seen adjacent to a fragment of myxoid tissue.

May-Grünwald-Giemsa stain × 100.

Table 1 *Initial cytological reports from aspiration biopsy in 31 histologically verified primary adenoid cystic carcinomata*

Initial cytological diagnosis	Time of cytological diagnosis	
	1953–1965	1966–1967
Cyst	1	–
Pleomorphic adenoma	13	1
Carcinoma	8	–
Adenoid cystic carcinoma	–	8
Total	22	9

1965 and one in 1966 Carcinoma was cytologically reported in eight cases all from the first period, and the cytological diagnosis was adenoid cystic carcinoma in eight cases, all from 1966–1967

The cells aspirated from the adenoid cystic carcinomata had round or oval nuclei surrounded by a scarcely detectable rim of cytoplasm (Fig 1 A) Cell size showed little variation. In addition to tumour cells, cylindrical structures —globules of mucus—were seen in the slides from 18 of the 31 adenoid cystic carcinomata (Fig. 1 A) Such globules were not seen in aspirates from the other salivary gland tumours, including the pleomorphic adenomata Their presence may therefore be regarded as indicative of adenoid cystic carcinoma (Eneroth & Zajicek 1969) This is important when the cytologist is otherwise in doubt as to whether he is dealing with a pleomorphic adenoma (mixed tumour) or a carcinoma. Recognition of malignancy will in such cases be based partly on the cells, but mainly on their mucinous product with its characteristic globules.

The presence of mucus globules suggests that the adenoid cystic carcinoma is of highly differentiated type (Eneroth *et al* 1967) The predominantly solid poorly differentiated adenoid cystic carcinomata in this study did not yield such distinct "cystic" (mucoid) aspirate.

In adenoid cystic carcinoma of low differentiation the recognition of malignancy is not difficult, but cytological typing of the tumour is not always possible In such cases, the cytologist can only report a carcinoma and the typing must await histological analysis, which may disclose predominantly solid adenoid cystic carcinoma.

Acinic-cell carcinoma Table 2 shows the initial cytological reports in the 28 cases of acinic-cell carcinoma Here too, the tumours are grouped according to the time of diagnosis. Benign epithelial tumour usually adenoma, was cytologically reported in 12 cases, 10 of them from the period 1953–1962 and two from 1963–1967 Carcinoma was cytologically suspected in two cases from the first period. Carcinoma without further specification was reported in three cases. Acinic-cell carcinoma was suggested or diagnosed in 11 cases, seven of them from the second period of the study The review of the slides showed that the smears from acinic-cell carcinomata characteristically contained clusters of cells with central nuclei and abundant foamy cytoplasm Generally no clear-cut cellular atypia was seen, and the diagnosis was based on the presence of numerous acinic cells in solid plugs with total absence of ductal epithelium (Fig 1 B)

Other adenocarcinomata From the five mucus-producing adenopapillary adenocarcinomata and the single trabecular adenocarcinoma, abundant tumour material was obtained The aspirate consisted partly of plugs of overlapping cells and partly of sheets of cells in more regular arrangement. The individual cells in

Table 2 *Initial cytological reports from aspiration biopsy in 28 histologically verified primary acinic-cell carcinomata*

Initial cytological diagnosis	Time of cytological diagnosis	
	1953–196	1963–1967
Benign epithelial tumour	10	2
Suspectedly malignant epithelial tumour	2	–
Carcinoma type unspecified		1
Acinic-cell carcinoma	4	7
Total	18	10

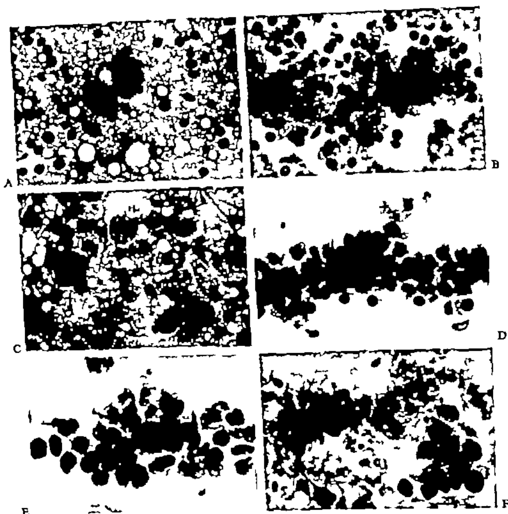


Fig. 1 A–F

Aspiration-biopsy smear from:

A. Adenoid cystic carcinoma showing two pink stained globules of mucus surrounded by carcinoma cells

B. Acinic-cell adenocarcinoma. A cluster of carcinoma cells exhibiting round nuclei and somewhat foamy cytoplasm is shown.

C. Adenopapillary mucus-producing adenocarcinoma. Carcinoma cells exhibit round nuclei surrounded by large amount of cytoplasm. In one of the cells a globule of mucus-like material is seen.

D. Muco-epidermoid carcinoma of low malignancy. A cluster of carcinoma cells with moderate nuclear atypia is shown.

E. Low-differentiated carcinoma. Pronounced nuclear atypia with decreased nuclear/cytoplasmic ratio is seen.

F. Low-differentiated carcinoma arisen in a pleomorphic adenoma. A plug of polymorphic carcinoma cells is seen adjacent to fragment of myxoid tissue.

May-Grünwald-Giemsa stain × 100.

he mucus-producing adenocarcinomata exhibited abundant cytoplasm and occasionally contained globules of mucus-like material, which appeared intensively red in MGG-stained smears (Fig. 1 C)

Muco-epidermoid carcinoma. In the muco-epidermoid carcinomata of low malignancy (18 cases) the aspiration biopsy usually yielded cystic fluid containing cell detritus and inflammatory cells, mainly lymphocytes. The carcinoma cells were of monomorphic appearance (Fig. 1 D) and resembled to some extent the oncocytes in papillary cystadenolymphomata. Definitive differentiation towards squamous epithelium was only rarely recognized in the smears. In the muco-epidermoid carcinomata of high malignancy grade (2 cases) by contrast, the cells were markedly polymorphic, and some of them strongly resembled the cells usually aspirated from squamous-cell carcinomata.

One diagnostic difficulty in muco-epidermoid carcinoma of low malignancy is that aspiration not infrequently yields only cystic fluid (in seven of our 18 cases) A cytological report of acellular fluid thus does not preclude tumour However when the fluid has been removed by aspiration, the clinical observations can be re-assessed. If the swelling disappear and other palpatory findings return to normal, the patient may as a rule, be freed from follow-up But if any suspicion of a lesion remains, the aspiration biopsy should be repeated, and, if the cytologic examination again shows no tumour cells, the case should be referred for surgical exploration.

Undifferentiated carcinomata. In the undifferentiated carcinomata, the cytologic picture was usually that of poorly differentiated or anaplastic carcinoma with a decrease in the cytoplasmic/nuclear ratio (Fig. 1 E) Six of these 15 carcinomata arose in pleomorphic adenoma. In four of the six cases, the aspiration-biopsy smears showed *only* carcinoma cells, and in the other two cases there were carcinoma cells *and mesenchymal elements* (Fig. 1 F)

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VARIATIONS IN RADIOSENSITIVITY OF VARIOUS TYPES OF MALIGNANT SALIVARY-GLAND TUMOUR

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The radiosensitivity of five different types of malignant salivary gland tumour—adenoid cystic, acinic cell, muco-epidermoid, mucus-producing adenopapillary carcinoma and carcinoma in pleomorphic adenoma—has been studied on the basis of the criterion "palpable tumour which was not definitely palpable 6 weeks after the end of radiation therapy In a series of 1678 cases of parotid tumour all patients who had received uniform radiation therapy were investigated

In a retrospective study of parotid tumours in 1678 patients seen at Radiumhemmet, Stockholm from 1909 to 1958 the object was to *analyse the radiosensitivity of malignant parotid* tumours

MATERIAL AND METHODS

A histological reclassification according to modern *nomenclature (Eneroth, 1964) was made* of all tumours. The prerequisites for a histological re-examination existed in all these 1678 cases, since slides and tissue blocks are filed at the Institute of Radiopathology Stockholm After histological re-examination of the 1687 tumours, 299 were classified as malignant. Fifty-one patients with malignant parotid tumours who had received uniform pre-operative irradiation were investigated. Of these 51 patients, nine had adenoid cystic, 10 acinic cell, 19 muco-epidermoid nine mucus-producing adenopapillary carcinomata, and four carcinomata in pleomorphic adenoma

If a tumour that was easily palpable at the first examination was not definitely palpable 6 weeks after the end of radiation therapy the radiosensitivity was considered to be high. The pre-operative irradiation was given by short-distance techniques, either by using teleradium units or ^{60}Co units with 6 to 7 cm between the radiation source and skin (Walstam, 1965). One circular field, 6 cm in diameter was used. The dose maximum at 2 mm depth was calculated to be 2600 to 5000 rads. It was possible to calculate the dose *at different depths* throughout the tumour mass fairly accurately The dose at 1 2 and 3 cm depth was *2100–4300 1600–3700 1200–3500 rads,* respectively

RESULTS

In four of the nine cases of adenoid cystic carcinoma and in three of the 10 cases of acinic *cell carcinoma, the tumour disappeared* clinically in the course of 4 to 6 weeks after treat

Table 1 *The radiosensitivity of five different types of malignant salivary-gland tumours*

	Radio-sensitive	Not Radio-sensitive	Total
Adenoid cystic carcinoma	4	5	9
Acinic-cell carcinoma	3	7	10
Muco-epidermoid carcinoma	0	19	19
Carcinoma in pleomorphic adenoma	0	4	4
Mucus-producing adenopapillary carcinoma	0	9	9

ment (Table 1) At subsequent operation mere ly small non-palpable residues were present. The other 12 cases of these two malignant parotid tumours presented evidence of only moderate or no regression after pre-operative irradiation. In none of the 19 cases of mucoepidermoid carcinoma, the four cases of carcinoma in pleomorphic adenoma and the nine cases of mucus-producing adenopapillary carcinoma did the tumour disappear clinically within 6 weeks, pre-operative irradiation producing only moderate or no regression.

DISCUSSION

Very little is known of the radiosensitivity of malignant salivary-gland tumours. In the present large series of patients with malignant parotid tumours who had received uniform radiation therapy there was a possibility of studying the radiosensitivity of malignant salivary-gland tumours.

According to estimates from a number of workers the radiosensitivity of adenoid cystic carcinomata varies widely (Ahlbom, 1935 Baclesse, 1946 Foote & Frazell, 1954 Berdal & Mylius, 1954 Blanck *et al* 1967) In this investigation adenoid cystic carcinoma appeared to be one of the more radiosensitive malignant parotid tumours. In four of the nine cases, the tumour disappeared clinically in the course of 6 weeks after treatment.

Some authors (Grage *et al.*, 1961 McCabe & Boles, 1962) have stated that acinic-cell carcinoma has low radiosensitivity others (Eneroth *et al.* 1966) that there is a possibility of influencing this type of tumour by radiation therapy In our series, acinic-cell carcinoma is close to adenoid cystic carcinoma in radiosensitivity Three of 10 tumours showed marked radiosensitivity

Most authors (Stewart *et al.* 1945 Linell, 1948 Marcial-Rojas & Sommers, 1954 Patey 1965 Jakobsson *et al.*, 1968) state that mucoepidermoid carcinoma is of relatively low radiosensitivity In none of the 19 muco-epidermoid carcinomata did the tumour disappear clinically within 6 weeks after irradiation. Neither did the nine mucus-producing adenopapillary carcinomata, nor the four carcinomata in pleomorphic adenoma given pre-operative irradiation with the same technique show any radiosensitivity This is in agreement with other authors (Eneroth *et al* 1968 Blanck *et al.*, 1967)

No definite conclusions as to the radiosensitivity of these five different types of malignant salivary-gland tumours could be drawn from the present series, but adenoid cystic and acinic cell carcinomata seem to be the more radiosensitive types of malignant salivary-gland tumours.

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CYTOLOGICAL ASPIRATION BIOPSY IN OTORHINOLARYNGOLOGICAL PRACTICE

A PRELIMINARY REPORT WITH SPECIAL REFERENCE TO METHOD

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The material consists of 128 lesions in the head and neck, 52 of which were salivary-gland lesions. A Millipore-filter technique was used in collecting cytological material. With this technique it is, on the other hand, possible to collect even very scanty amounts of cellular material, and, on the other preservation of cells and good staining properties are ensured. So far histological verification has been performed in 62 of these cases. As to malignancy false positive diagnoses were made in 2.3 per cent and false negative diagnoses in 5.5 per cent of the cases.

Studies on aspiration biopsy were performed as early as the 1930's (Martin & Ellis, 1930 1934) but as a diagnostic tool it was first used systematically by Swedish scientists in the 1950's. Mavec, Eneroth and others investigated aspiration biopsies of salivary gland (Mavec *et al.* 1964 Eneroth *et al* 1965 1966 1967), Franzén and Esposti and their co-workers studied those of the prostate (Franzén *et al.* 1960 Esposti, 1960 Esposti *et al* 1960) Einhorn & Franzén studied the thyroid gland (1962), Zajicek *et al* (1967) the mammary gland, and Nasiell (1967) studied lung tumours. In addition, Söderström published a comprehensive monograph on aspiration biopsy (1966) In the above-mentioned studies only—or primarily—the haematological method was used, i e the cytological smears were dried and stained according to the May-Grünwald-Giemsa method (with the exception of Nasiell's study)

In the Second Department of Pathology at Helsinki University (and later also in the Central Laboratory of Pathology founded in 1967) cytological aspiration biopsies have been studied since 1959 First, samples were taken from lung tumours and then (since 1966) from the prostate, mammary gland, kidney pancreas and lymph nodes (data on these are to be published later) In otorhinolaryngological practice some aspiration biopsies were done in 1966 but systematic investigations were not performed until the beginning of 1968

METHOD

The samples were taken with the instruments developed by Franzén, and the biopsy technique was the same as in the publications mentioned above. The cellular material was delivered from a syringe into a sample tube containing 5–10 ml of 50 per cent ethanol, with which the syringe and needle were also rinsed so as to remove the cellular material as carefully and thoroughly as possible. When the first sample was heavily contaminated with blood or seemed scanty a second sample was in some cases taken at once The cellular material was allowed to remain in the fixative (50 per cent ethanol) for a few hours, where after the material was collected on to a Millipore filter The filter was fixed and stained according to the Papanicolaou technique, specifically modified for Millipore filter The apparatus consisted of an ordinary rectangular filter holder and rectangular filters (pore size 5 or 8μ) When preparing specimens with scanty cellular material, the authors employed a special inner funnel of plastic, by means of which the cel-

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lular material was concentrated to the centre of the filter over a round area, 12 mm in diameter so as to make the screening of these samples easier The rectangular stained filters were mounted with Permount between the object and cover glass.

MATERIAL

The samples were collected in the routine work at Helsinki University ENT Clinic from vari ous lesions in the head and cervical region, particularly when a tumour was suspected. By May 1969 we had samples from 128 cases, viz. from 52 salivary-gland lesions, 69 lesions in the cervical region (enlarged lymph nodes and other lesions) and seven other lesions in the mouth and pharynx. So far histological studies have been performed in 62 of the cases

RESULTS

In 19 og the *salivary-gland* samples, the cytological findings indicated mixed tumour Of these cases, 10 have been verified histologi cally In the remaining nine cases a firm encapsulated tumour suspected to be mixed tu mour was found in the clinical investigation. Two of the 10 cases investigated histologically were found to be malignant (infiltrative growth) One of these had already been found to be malignant in the cytological investiga tion, whereas the cellular picture of the other case was considered benign. In only one case of mixed tumour was the aspirated cellular material so poor that no diagnosis could be made cytologically

In addition to mixed tumours, the salivary gland material contained four other tumours Two were histologically verified adenoid cystic carcinomata. Both of them were also cytologi cally considered to be malignant one had been classified properly in the cytological investiga tion in the other case however anaplastic carcinoma had been suggested. The remaining two were acinic-cell tumours one of them was malignant (cytological sample acellular) and the other was the rare benign variant (cytologically acinic-cell tumour probably malignant).

Finally in one case, the cytological diagnosis was cystadenolymphoma, but the operation has not yet been undertaken, and so the case remains histologically unverified.

The remaining 27 salivary-gland samples were taken from benign non-neoplastic lesions. These lesions were also diagnosed to be benign cytologically except for one case of Mikulicz's disease, which was at first suspected to be a lymphoma, in a second aspiration biopsy a benign inflammation, and only histologically was the diagnosis of Mikulicz's disease established. For obvious reasons, the histological confirmation was performed only in nine of these benign lesions.

Of the lesions in the *cervical region* (69 cases) 57 were enlarged lymph nodes. On the basis of the cytological findings 23 were considered or suspected to be malignant (19 metastatic carcinoma, 4 lymphoma) All the metastatic carcinomata were verified histologically and so were two additional cases in which the cytological findings had been negative. In one case, the sample was acellular and in the other case the first sample was negative, while the control sample indicated malignancy In addition to these two false negative diagnoses, there was one false positive cytological lymphoma diagnosis Clinically this case was suspected to be malignant, but the histological biopsy showed only atypical hyperplasia.

Twenty-six lymph node samples were cytologically benign or inadequate (18 and 8 respectively) Ten of these were studied histologically and in the remaining 16 cases the lesion was considered to be benign on the basis of the clinical investigation.

Of the other lesions in the cervical re (12 cases) seven were histologically confin cysts, four of which had already been d nosed on the basis of the cytological findi In three cases, however the cytological samples had been completely acellular Of the re maining five cases, four were both cytologically and histologically found to be benign thyroid

gland nodes. Finally one neurilemmoma had been cytologically diagnosed as benign mesenchymal tumour

In seven cases, aspiration-biopsy samples were taken from the *mouth or pharynx*. In five cases, the cytological diagnoses were verified histologically: two malignant lympho-epitheliomata in the pharynx and three benign inflammatory lesions. In one of the two remaining cases the cytological sample showed malignancy in agreement with the clinical diagnosis. Histological verification is not yet available. In the seventh case, the lesion was found to be benign.

DISCUSSION

In our experience the Millipore technique is better than ordinary smear preparations when using the Papanicolaou staining method, because

– the cellular material is fixed immediately "in situ" i. e three-dimensionally which ensures excellent preservation of cells and facilitates comparison between cytologic and histologic preparations,

– cellular material does not remain in the syringe, as the syringe is rinsed with the fixative, which is not done in the smear technique,

– the drying of cellular material is efficiently avoided. The staining properties of dried smears are poor in the Papanicolaou technique, and so interpretation is made more difficult or even impossible

– material from several aspirations can be collected on the same filter and is consequently easier to study

So far our material is so limited that no definite conclusions can be drawn. A review of the results shows that satisfactory samples were obtained in 114 out of 128 cases (89 per cent): the acellular samples were rare in parotis cases (two out of 52, i. e. 4 per cent) and more common among cysta colli samples (three out of 12, i. e 25 per cent). As to malignancy false positive diagnoses were made in three cases (2.3 per cent) These occurred at the beginning of this work when our knowledge of cytological pictures of this kind of aspiration biopsies in Millipore technique was scanty False negative diagnoses were made in seven cases (5.5 per cent) In three cases, the false negative diagnosis was due to an acellular sample. These results agree, on the whole, with the results found in the literature (e. g. Eneroth *et al* 1967)

A description of the morphology will be published later in connection with the results of a more comprehensive material.

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DISCUSSION

H Diamant What do you mean when you say Mikulicz s disease? I have for at least 10 years avoided this name and so has a lot of other people working in this field I think that it has very little meaning and that it should be removed from our terminology

E Holopainen (Reply to Diamant) We have used this diagnosis in the clinical work as well as in histopathology As long as the aetiology and the pathogenesis of these collagenous diseases are unknown, this diagnosis may be considered reasonable.

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THE SIGNIFICANCE OF THE AUTONOMIC INNERVATION FOR THE SALIVARY SECRETION IN THE HUMAN PAROTID AND SUBMANDIBULAR GLANDS

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The distribution of sympathetic and parasympathetic nerves in human salivary glands has been studied histochemically and electron-microscopically Both glands are innervated by sympathetic (noradrenaline containing) and parasympathetic (cholinesterase-containing) nerves. The sympathetic nerve terminals may also be identified by their content of vesicles of special type. The morphological findings permit the conclusion that the adrenergic transmitter noradrenaline can probably reach all acinar cells as well as the myo-epithelial cells. A large proportion of the effector cells can evidently also be influenced directly by the parasympathetic transmitter acetylcholine.

Salivary secretion is impaired by surgical or pathological damage of the parasympathetic nerves innervating the salivary glands. Especially the chorda tympani, which contains the parasympathetic outflow to the submandibular gland, is open to injury by such conditions as surgery of the stapes, radical operation for chronic otitis, idiopatic facial nerve paresis and skull fractures.

It is obvious that salivary secretion is controlled by the autonomic nervous system, but the relative importance of the sympathetic and parasympathetic nerves has not been established. Thus, while the parasympathetic nerves evidently are the main secretory nerves, the importance of the sympathetic nervous system is obscure

One way to start an elucidation of these problems is to study the distribution of parasympathetic and sympathetic nerves in the salivary glands. In the present investigation, three techniques were used to study the sympathetic innervation (fluorescence histochemistry according to Falck, 1962 and Falck *et al.*, 1962) parasympathetic innervation (cholinesterase staining) and ultrastructure of the autonomic nerves (electron microscopy using potassium permanganate according to Richardson, 1966) A full account of this investigation with the three techniques has been given by Eneroth *et al.* (1969).

Fluorescence microscopy revealed a rich net work of sympathetic nerve terminals enclosing the acini of both submandibular and parotid glands. Cholinesterase staining resulted in a similar picture, a network of parasympathetic nerve terminals enclosing the acini.

The electron-microscopic studies permitted selective identification of sympathetic and parasympathetic nerves, the former containing dense cored (noradrenaline-containing) granules with a diameter of about 500 Å. Both sympathetic and parasympathetic nerves were found mostly to run in the same Schwann cells, and thus probably reach the same effector cells. This observation supports the view that the acini of the salivary glands are doubly innervated by both the sympathetic and the para sympathetic nervous system.

The abundant occurrence of both sympathetic and parasympathetic nerve terminals innervating the acinar cells strongly indicates that both types are of functional importance. In the light of these results and functional observations in other mammals, it seems highly probable that the sympathetic nerves can also induce salivary secretion. Thus, it is probable that the

DISCUSSION

H Diamant What do you mean when you say Mikulicz s disease? I have for at least 10 years avoided this name and so has a lot of other people working in this field I think that it has very little meaning, and that it should be removed from our terminology

E Holopainen (Reply to Diamant) We have used this diagnosis in the clinical work as well as in histopathology As long as the aetiology and the pathogenesis of these collagenous diseases are unknown, this diagnosis may be considered reasonable.

Acta Otolaryng. 263 193–194 1970

THE SIGNIFICANCE OF THE AUTONOMIC INNERVATION FOR THE SALIVARY SECRETION IN THE HUMAN PAROTID AND SUBMANDIBULAR GLANDS

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HORMONAL SIALOSIS DURING TWO CONSECUTIVE PREGNANCIES

J Udsen and K. A. Thomsen

From the Department of Otolaryngology the University Hospital Copenhagen, Denmark

During her first pregnancy a 17-year-old woman revealed distinct bilateral swelling of the parotid glands. The swelling was believed to be of hormonal origin and subsided spontaneously after delivery During her next pregnancy year later a similar swelling occurred.

A woman, aged 17 was examined in April 1967 a few days after her first delivery At this time there was distinct swelling of the parotid glands. Palpation revealed that the glands were firm, homogeneous and indolent.

In March 1967 the patient had been examined in a local hospital, because of bilateral swelling of the parotids, which had begun in the first trimester of her pregnancy Her complaints were only of a cosmetic nature specifically there was no oral dryness or salivation. Serological tests (differential count, haemoglobin, sedimentation reaction, MCV MCHV leukocytes, eosinophils, platelets, electrophoresis) showed no abnormalities. An examination by the internist was arranged, but the patient did not come.

In our department, all the blood tests were repeated, and AGKT ANF LE cells, AST and serum amylase were also analysed. All tests as well as chest radiography showed normal conditions. Sialography of the parotid glands was planned, but again the patient failed to attend.

The patient was examined again shortly after her second delivery in March 1968 and again pronounced bilateral swelling of the parotids was present. The patient informed us that the swelling had subsided quickly after the first delivery and that the glands became perfectly normal for a few months until the first trimester of her second pregnancy when bilateral swelling of the parotid region reappeared. She had no other complaints.

As the literature gives only a few examples of this disease, we find that this case may be of interest.

remaining secretion which is found after damage of the parasympathetic nerves is caused largely by sympathetic nervous activity and not by endocrine factors.

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SURGERY OF THE CHRONIC EAR

Film

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From the University Department of Otolaryngology Oulu Finland

The film can be obtained from the Astra Film Library Södertälje Sweden

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INTUBATION IN MAXILLARY SINUSITIS

Film

P Knudstrup

From the University Department of Otorhinolaryngology Odense Denmark

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CLINICAL AUDIOMETRY ON GENERAL PURPOSE COMPUTER (IBM 1800)

Film

G. Salomon

*From the Departments of Otolaryngology and of Data Processing in Medicine
Copenhagen County Hospital, Gentofte Denmark*

Acta Otolaryng 263 200–204 1970

DIPHASIC IMPEDANCE CHANGE AND ITS APPLICABILITY IN CLINICAL WORK

G Flottorp and G Djupesland

From the Department of Otolaryngology and the Institute of Audiology Rikshospitalet, Oslo Norway

In 186 ears of 115 patients, impedance changes at the onset and at the end of the stimulus ("diphasic impedance changes") were recorded, using Madsen Impedance Instruments Model ZO 61 and Model ZO 70 The eliciting stimuli were·

1 Tactile stimulus
2. Acoustic stimulus
3 Defensive-reaction or startle-evoking stimulus

In some cases, all three stimuli evoked diphasic impedance changes. In most cases, however only stimuli 2 and 3 or stimulus 3 alone, produced such changes. A combination of monophasic and diphasic impedance change was never observed in one and the same ear Diphasic impedance change was always found to represent two successive, transitory reductions of the middle-ear impedance Based upon the observed pattern of the impedance change it is suggested that the change is caused by a special type of movement of the ossicular chain, found in ears with otosclerosis. The more advanced the state of otosclerosis, the more vigorous is the stimulus necessary to elicit the diphasic change. We have found this pattern of impedance change useful as a diagnostic aid

At the VII International Congress of Audiology in Copenhagen, 1964 Terkildsen (1964) stated the following regarding impedance changes elicited by middle-ear muscle activity· As a rule, the intra aural muscle reflexes are absent in patients with otosclerosis. In rare cases, there may be a muscle response, but only as a momentary burst at the onset of sound and again when the sound is turned off This on-off reflex can only be caused by the tensor muscle" At the same Congress (1964) we presented a few cases in which a similar on-off phenomenon had been observed, hereafter called diphasic impedance change" We have since continued our study looking for patients in whom a diphasic impedance change could be elicited

MATERIAL AND METHOD

From 1962 to 1969 we found diphasic impedance change in 186 ears of 115 patients. *Table 1* shows the distribution of the material of which 63 per cent were females 83 per cent were between the ages of 30 and 59 years. The diagnosis was based on the history clinical examination of the ear nose and throat, and audiological findings Of the patients, 112 suffered from otosclerosis. The diagnosis was verified by surgery in 59 cases. In six of these cases otosclerotic foci were found by histological examination of the removed stapes plate In addition to otosclerotic findings, two patients exhibited osteogenesis imperfecta (blue sclerae,

Table 1 Distribution of the 115 patients according to age and sex

Age in years	Male	Female
0– 9	1	1
10–19		1
20–29		8
30–39		10
40–49		27
50–59		15
60–69		7
70–79		
80–89		1
Total	4	72

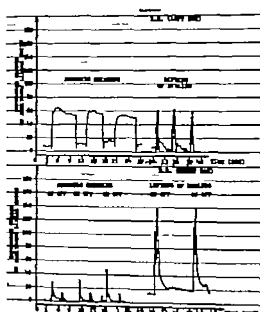


Fig. 1 Example of monophasic impedance change (left ear of one patient) and diphasic impedance change (right ear of the same patient).

one ear operated) and one exhibited a typical Cogan s syndrome.

The impedance changes were recorded by a modified Madsen Acoustic Impedance Meter Model ZO 61 This apparatus has previously been described by Djupesland (1967) In addition, the Madsen Electro-Acoustic Impedance Bridge, Model ZO 70 was employed for the last 30 patients. Both ears of each patient were examined. In approximately half of the patients, impedance changes were recorded on a Brüel and Kjær Level Recorder (2405 A) using a linear potentiometer Movement of the indicator needle on these impedance instruments also provided an easy observation of the form of the impedance change.

Impedance changes were investigated with the use of the three main types of stimulus regularly applied to patients in our clinic:

1 Tactile stimulus, ipsilateral and contralateral, touching the skin around the opening of the external auditory meatus with a piece of cotton wool.
2. Acoustic stimulus, using Bárány s noise box and pure tones.
3 Defensive-reaction or startle-evoking stimulus, consisting of a sudden strong lifting of the upper eyelids. The thumbs of the examiner resting lightly against the lids, are pressed suddenly upward and inward.

The impedance changes were correlated with the type and degree of hearing loss in order to give the study clinical applicability

RESULTS

The pattern of the impedance change (Fig. 1) served to divide our results into two main groups (Fig. 2.)

1 Normal, monophasic impedance change
2. Abnormal, diphasic impedance change.

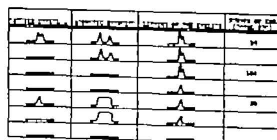


Fig. 2. Distribution f response patterns recorded in the 230 ears examined.

(In some cases, we saw the first phase being split up (Fig. 3 d.) thereby producing a virtually triphasic pattern, however we counted these as diphasic in the sense that they are different from the monophasic type.)

The most remarkable result is probably that we never found a combination of monophasic reaction to one stimulus and a diphasic pattern to another in one and the same ear In other words, a diphasic pattern may be seen in combination with no change, but never together with a monophasic change.

The diphasic impedance change may present itself in various patterns:

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Total	43	72

effect) and a larger change at the end of the stimulus (large off-effect) (Fig. 3 c)

A split impedance change at the beginning (split on-effect) together with a normally shaped, but smaller change at the end (small off-effect) (Fig. 3 d) This pattern was rarely seen.

By means of the Madsen Electro-Acoustic mpedance Bridge, Model ZO 70 it was possible to determine the direction of the impedance change. In normal ears, with normal middle-ear pressure we always observed that the monophasic impedance change represents a transitory increase of the impedance (higher acoustic ohm, less compliance) The diphasic impedance change however always consists of two components of decreased impedance separated in time by a value being either normal or increased. We were unable to examine the direction of the impedance change in all patients, since the impedance bridge ZO 70 was available only during the last part of this study However so far there has been no exception from the mentioned pattern.

Some of our patients were able to observe a momentary loudness increase of the low-frequency probe tone in conjunction with the diphasic pattern. In cases of monophasic impedance change, many of our patients observed a decrease in loudness However most patients seem to be unable to observe any loudness change at all in connection with an elicited impedance change.

In patients having had a successful stapedectomy diphasic impedance changes were elicited, but only by lifting the upper eyelids.

If we try to correlate the pattern of impedance change with the degree of hearing loss in the examined ear it is found that diphasic change for all three stimuli is only seen in patients with negligible hearing loss in that ear In the other ear of these patients we always found a greater hearing loss of the otosclerotic type. As the hearing loss increases first the reaction to the tactile stimulus disappears then the acoustically elicited diphasic changes vanish. Only in very rare cases was it impossible to elicit diphasic impedance change by lifting the upper eyelids. Today we have some doubt as to whether it should not be possible to elicit impedance changes also in these cases when the stimulus is properly applied.

DISCUSSION AND CONCLUSIONS

Without trying to explain the mechanism responsible for the diphasic pattern, we think our results indicate that the observed pattern is caused by a special type of movement of the ossicular chain, due to action of either the stapedius muscle or the tensor tympani muscle or both muscles in co-operation. It can hardly be due to any artefacts in the measuring instrument itself caused by a variation of the impedance vector being transformed by the instrument to a variation on a linear scale. Since a diphasic impedance change is seen in operated ears in which the tendon of the stapedius muscle has been cut, the tensor muscle solely must be able to produce the special movement of the chain. On the other hand, the fact that tactile stimulation of the meatus (known to activate only the stapedius muscle Djupesland, 1967) is able to elicit the diphasic pattern indicates that the stapedius muscle must also be able to perform the action producing the diphasic change. The diphasic pattern may be produced as a result of an inward movement of the tympanic membrane together with a change in the shape of the tympanic membrane Such a movement might increase temporarily the volume in the ear canal without increasing the stiffness of the eardrum and the ossicular chain, resulting in the very special impedance values seen at the onset and at the end of the stimulus. However it seems more likely that the ossicular chain itself is temporarily in a condition producing greater conductivity for the vibrations (smaller impedance value) at the onset of the stimulus and at the end of the stimulus. This may be comparable to Klockhoff's finding (1961) that most tensor responses in genuine stapes ankylosis are as-

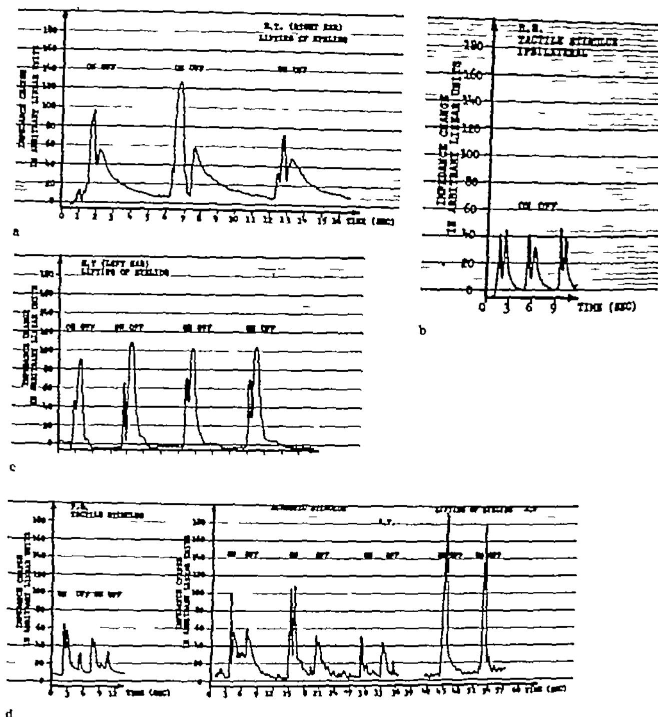


Fig. 3 Various patterns of the diphasic impedance change
a. *Great change at the beginning, small change at the end of the stimulus.*
b Almost equal changes at the beginning and end of the stimulus.
c. Small change at the beginning, greater change at the end of the stimulus.
d. Split change at the beginning, normal change at the end of the stimulus (only seen for tactile and acoustic stimuli).

1 A large change at the beginning of the stimulus (large on-effect) and a small change at the end of the stimulus (small off-effect) (Fig 3 a)

2 Almost equal changes at the beginning and the end of the stimulus (equally large on- and off-effects) (Fig. 3 b)

3 A small change at the beginning (small on-

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IMPEDANCE MEASUREMENTS

PROBE TONE INTENSITY AND MIDDLE EAR REFLEXES

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Eleven normal subjects were examined by the impedance method with respect to the influence of probe tone intensity on the middle ear muscle reflexes. If the probe tone is reduced from 70 dB sensation level to 60 dB SL, the threshold tends to become higher and the reflexes are smaller. This holds for reflex eliciting stimuli up to around 95–100 dB. With stronger stimuli, the reflexes become stronger with weak probe tones. Thus, exact knowledge about probe-tone intensity is important for accurate evaluation of the middle-ear muscle reflexes by the impedance method.

It is well known that the middle-ear muscles in man can be activated in several ways.

The acoustic reflexes involve only few synapses, and they might be designated as a primary type of response, in contrast to reflexes that are induced by tactile stimulation or as part of particular activity patterns in muscles of the head or the neck. Furthermore there is no doubt that other conditions, such as mental activity, previous experience with intense listening, noise exposure and emotional attitude are of some importance. All these factors interact mutually in a complex manner that can best be described in terms of habituation or facilitation.

When the middle-ear muscle reflexes are measured by means of the impedance method, the so-called indicator ear is submitted to tactile stimulation from the insert tip and at the same time to an acoustic stimulus by the probe tone. The tactile sensation will elicit a contraction which vanishes within seconds through habituation. The probe tone is of an intensity which is considerably below the reflex threshold at this frequency. With the knowledge we have about mutual facilitation or blocking of the habituation process, when several modes of stimulation are applied at the same time, even if they are at a subliminal level, it is of interest to see what influence the probe-tone intensity may have on the reflexes.

The Madsen ZO-70 impedance apparatus is well suited for such an investigation. The probe-tone intensity at the ear-drum is always the same, when the cursor scale has been adjusted to obtain a zero balance. Due to the measuring principle, there is a linear relation between changes of the ear-drum impedance and the magnitude of deflection which is measured by means of the apparatus. In the commercial apparatus, the probe-tone intensity is 65 dB SL. We had a model adapted, so that it was possible to choose between two probe-tone intensities, 60 dB and 70 dB. A single switch sufficed to shift the intensity. It was ascertained through measurements that the linear characteristics remained unchanged with both intensities. At 220 cps, 70 dB SL is still 10–15 dB below the reflex threshold. During the investigation we found no reason to suspect that this did not hold true, and there was no indication of a reflex when the probe tone was shifted from weak to strong. The reflexes were recorded by means of a Mingograph 81.

It was decided to use the frequencies 250 and 1000 cps as reflex-eliciting stimuli in the contralateral ear. Each tone was presented automatically with a duration of 5 sec, rise-decay time 25 msec, and intervals between 15–20 sec.

sociated with a transient impedance decrease

However at the present time it is of greater interest to examine the correlation between *the diphasic impedance change and the type of* hearing loss present. Since we have so far seen diphasic impedance changes only in connection with otosclerotic ears, or ears that may probably be compared mechanically with otosclerosis (no movement of the stapes foot plate, either caused by fixation or by defective crura) it is likely that this special impedance pattern is pathognomonic of otosclerosis. It has been found at all stages of hearing loss result ing from otosclerosis, the pattern of the elicited impedance change being the same However the possibility of eliciting it varies with the de gree of hearing loss In more advanced stages, the diphasic impedance change can be elicited only by means of the rather strong stimulus that leads to the defensive reaction i. e vigor ous lifting of the upper eyelids.

We have found this impedance pattern valuable in identifying otosclerosis in its earliest stages Especially in cases in which the size of the air bone gap is so small that it is in reality doubtful or in which otosclerosis is combined with a sensory neural hearing loss, we have found it useful to have this objective registra tion to solve differential diagnosis problems.

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DISCUSSION

G Lidén We consider the acoustic middle-ear reflex test very useful in separating conductive lesions from sensorineural impairment. We have observed responses" in some cases with otosclerosis, but these were due to interactions between stimulus tone and probe tone

G Flottorp (Reply to Lidén) Diphasic impedance changes have been elicited in otosclerotic ears at stimulus intensities varying with the hearing loss present In cases with normal and near normal hearing in the stimulated ear we have elicited diphasic impedance changes at normal impedance threshold i e at sound-pressure levels from 80–90 dB It should probably be emphasized that we have always seen diphasic impedance changes represent a transitory *decrease* in the impedance, while the normal monophasic changes have always been a transitory *increase* in the impedance.

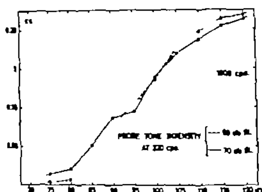


Fig. 3.

weak probe tone are smaller up to a stimulus intensity of 95–100 dB, and above this level they are larger The difference is statistically significant for stimulus levels 90 dB and 105 110 and 115 dB.

It is evident that a statistical evaluation for the low stimulus intensities loses its meaning simply because there are so few results never theless the probe-tone intensity appears to have its largest influence just here.

Our results show that the probe-tone intensity is important when the middle-ear muscle reflexes are evaluated by means of the impedance method, both with regard to the reflex threshold and the magnitude of the reflexes above the threshold. Near the threshold the probe tone appears to *facilitate* the reflex in spite of the fact that its intensity is considerably below the reflex threshold. It is difficult to explain why the reflexes at high stimulus intensities are stronger with a weak probe tone. It might be assumed that the strong probe tone would cause an increase of muscle tonus and in this way reduce the phasic response during a reflex. This explanation seems unlikely if it is remembered that the procedure involved very frequent shifts of probe-tone intensity and that these shifts caused no change in the stationary ear-drum compliance whatever Maybe we are concerned with some kind of habituation to strong tones, but at the present time this question must be left open.

DISCUSSION

G Salomon. Interaction between different types of stimulation of the middle ear muscles has also been demonstrated in cats (Salomon, G. 1966. Middle ear muscle activity *Proc Royal Soc 59* 966) As in your experiments, facilitation and inhibition were present, de pending on a variety of parallel stimuli. It may be appropriate to think of the middle-ear muscle reflex as guided by a sum of input stimuli, the power of each stimulus depending on the state of the CNS, and the habitual pat tern of reflex of each person.

I think that when Lidén found only tensor activity in response to sound in 20 % we must assume that in the other patients, although no tensor response to sound was demonstrated, an influence on the tensor mechanism must have taken place.

The registration was started at the reflex threshold for both frequencies with both probe tone intensities, and during the procedure there would be a continual shifting between the two probe-tone intensities and frequencies Maximum intensity for 250 cps was 105 dB and for 1000 cps 120 dB Each reflex represents the average of three consecutive measurements.

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Eleven normal persons were test subjects, six male and five females, age range 19–45 years with an average of 31 years It is our experience that persons employed in acoustic professions often exhibit reflexes to rather weak stimuli, and all the test subjects were naive

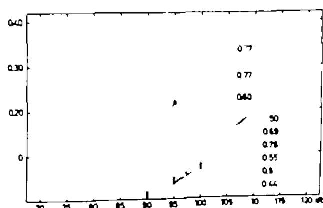


Fig. 1

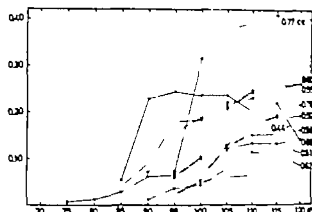


Fig. 2.

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Figs 1 and 2 show the reflexes for all 11 subjects The reflex magnitude is given as the shift of ear-drum compliance in absolute values Each point in the individual curve is an average of the results obtained with both weak and strong probe tones. The reflex elicited by a 1000 cps tone show large individual differences with regard to both the threshold the way it increases and the maximum value. For 250 cps it appears as if ears that exhibit a large change of compliance also tend to have a low reflex threshold

The average ear-drum compliance for all subjects was 0 61 cc with variations from 0 44 to 0 79 cc. The shift of compliance during a maximal reflex averaged 0 23 cc, with variations from 0 1 to 0 42 cc. It might have been expected that subjects with a large ear-drum compliance would also exhibit large shifts during a reflex There is such a tendency but it is not without exceptions. The person with the smallest reflex thus had an ear-drum compliance of 0 62 cc. There is also a tendency for patients with large ear drum compliance to have a reflex threshold at 250 cps that is lower than at 1000 cps.

Fig 3 shows the average curves for all subjects at 1000 cps with weak and with strong probe tones, respectively The reflexes with the

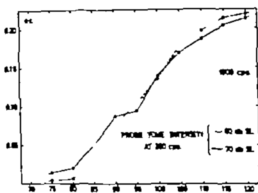


Fig. 3.

weak probe tone are smaller up to a stimulus intensity of 95–100 dB and above this level they are larger The difference is statistically significant for stimulus levels 90 dB and 105 110 and 115 dB

It is evident that a statistical evaluation for the low stimulus intensities loses its meaning simply because there are so few results never theless the probe-tone intensity appears to have its largest influence just here.

Our results show that the probe-tone intensity is important when the middle-ear muscle reflexes are evaluated by means of the impedance method, both with regard to the reflex threshold and the magnitude of the reflexes above the threshold. Near the threshold the probe tone appears to facilitate the reflex in spite of the fact that its intensity is consider ably below the reflex threshold. It is difficult to explain why the reflexes at high stimulus intensities are stronger with a weak probe tone. It might be assumed that the strong probe tone would cause an increase of muscle tonus and in this way reduce the phasic response during a reflex. This explanation seems unlikely if it is remembered that the procedure involved very frequent shifts of probe-tone intensity and that these shifts caused no change in the stationary ear-drum compliance whatever Maybe we are concerned with some kind of habituation to strong tones, but at the present time this question must be left open.

DISCUSSION

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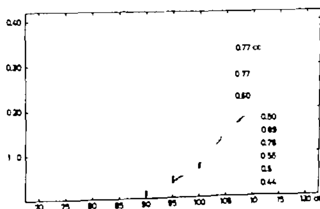


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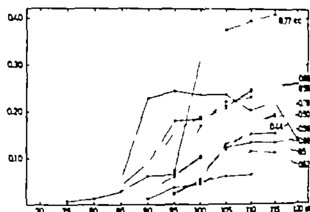


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the tympanic membrane in man is about as likely to suggest dominance of either the tensor tympani or stapedius muscle. However he pointed out that reversed manometric reflex reactions indicating a switch from negative pressure change to positive pressure change may be observed in some individuals. The reflex reversals may indicate predominant response of the other muscle or may be attributed to changed biophysical force vectors associated with the ossicular articulation. Furthermore, different patterns of cochlear stimulation may elicit variations in the responses of the two middle-ear muscles. Interfering bone conducted sound from the stimulated ear to the recorded ear might change the geometrical relationships of the stapes footplate and the ossicular joints and affect the instantaneous movements of the tympanic membrane accordingly

Tactile stimulation with an air-jet directed towards the orbital region homolateral to the ear from which reflexes are recorded is known to elicit a contraction of both muscles. This was predicted by Klockhoff in 1961 and subsequently verified upon surgery of the middle ear (Lindström & Lidén, 1964 Djupesland, 1967). Another technique which is considered to be a reliable method for eliciting the stapedial muscle reflex is touching the skin on the anterior part of the auricle of the homolateral ear with cotton wool (Djupesland, 1968)

Even though several techniques are used for eliciting the intra-aural muscle reflex and numerous studies have been reported, the behaviour of the middle-ear muscles to acoustic stimulation still remains somewhat of a mystery On the other hand, it is possible that measurements of relative impedance changes at the ear drum and eardrum movements can supplement each other and may provide more complete information as to the behaviour of the middle-ear muscles than if each dimension is evaluated separately For this reason, both methods were combined to obtain a simultaneous measurement. Thus, we shall report the results of simultaneously recording the relative impedance changes at the eardrum and eardrum movements during acoustic and non-acoustic stimulation. The purpose of this investigation was three-fold.

1 To clarify how the tensor muscle response appears in cases where the tensor is the only functioning muscle in the middle ear
2. to study the pattern of the intra-aural reflex during combined acoustic and orbital air jet stimulation and,
3 to determine if the tensor tympani muscle reflex can be elicited by acoustic stimulation, and if so to what extent.

EQUIPMENT

The equipment used in this investigation has been described in detail elsewhere (1969) Therefore only a brief description will be given here. The apparatus consists of four main parts (Fig. 1) the intra-aural reflex indicator a pressure-transducer system for extratympanic manometry a unit for changing and monitoring the air pressure in the ear canal for tympanometry and a four-channel graphic recorder At tached to a headband is a small metal case containing a receiver (miniature earphone) and a microphone. A two-pronged probe connected to these with rubber tubing is held in an air tight position in the ear canal by a soft foam-plastic cuff and a flexible locking arm described by Møller (1958) The probe tone has a fixed frequency of 800 Hz. The microphone monitors the sound pressure level of the probe tone in the ear canal between the tympanic membrane and the cuff

Intra-aural reflex indicator The reflex indicator consists of two electronic bridges. On its panel there are three indicating meters. The first meter monitors the sound-pressure level of the probe tone. Immediately prior to making a reflex measurement, the level of the probe tone is adjusted to 70 dB SPL on this *meter* In order to observe small changes in *amplitude* of the probe tone the second meter is connected to a DC-bridge permitting responses in either

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SIMULTANEOUS RECORDING OF CHANGES IN RELATIVE IMPEDANCE AND AIR PRESSURE DURING ACOUSTIC AND NON ACOUSTIC ELICITATION OF THE MIDDLE EAR REFLEXES

G Lidén J L. Peterson and E. R Harford

From the Departments of Audiology Sahlgren s Hospital Göteborg Sweden Louisiana State University School of Medicine New Orleans, Louisiana and Northwestern University Evanston Ill U S A

Intra aural reflex responses for normal and pathological human ears were obtained while utilizing equipment constructed at Sahlgren s Hospital. Acoustic and tactile stimuli were employed to elicit reflexes. Responses were displayed simultaneously on two channels of a graphic recorder indicating changes in *amplitude* and *amplitude phase* of an 800 Hz probe tone in the recorded ear Changes in air pressure in the same sealed auditory canal in response to middle ear muscle contraction were simultaneously recorded on a third channel. The response pattern on the impedance indicator and on the pressure transducer system during acoustic stimulation are primarily due to the stapedial muscle reflex. In a small fraction of the group of normal subjects (13 %) it appears that contraction of both middle-ear muscles was elicited by acoustic stimulation. In the group in which the tensor muscle was the only functioning muscle in the middle ear the tensor reflex could not be elicited by acoustic stimulation.

The elicitation of the stapedial and tensor tympani muscle reflexes by acoustic stimulation remains a controversial subject It is generally agreed that in animals both muscles perform reflex contractions on acoustic stimulation. It is intriguing that this does not also hold unequivocally in man.

Interpretation of middle-ear muscle activity is related to the method used for measurement. For example using either absolute or relative measurements for the acoustic impedance at the tympanic membrane it is possible to ascertain the presence of intra-aural muscle reflexes (Metz, 1946) However complete abolition of reflex responses was noted in patients with suprastapedial facial nerve lesions (Jepsen, 1955 Klockhoff 1961) In patients with paralysis of the trigeminal nerve, on the other hand the responses to acoustic stimulation were preserved (Metz, 1946 Lindström & Lidén, 1964) A conclusion to be drawn from these investigations is that during acoustic stimulation the stapedius muscle is the sole cause of the so-called intra-aural muscle reflexes in man at least as far as these can be ascertained through impedance measurements.

Another measuring method for studying the effect of acoustic stimulation on the middle-ear reflexes is to determine the movement of the tympanic membrane (extratympanic manometry) Assuming that the intra-aural muscles are acting antagonistically the tensor muscle pulls the eardrum inward while the stapedius muscle may cause movements in both directions, but mostly outward. If the external ear canal is sealed air tight, movement of the ear drum results in measurable changes in the air pressure within the canal Using different types of manometer systems, Mangold & Eckstein (1913) Terkildsen (1956 1957 1960) Mendelson (1957 1966) Holst *et al* (1963) and Weiss *et al* (1963) claimed to demonstrate contractions in the tensor tympani muscle during acoustic stimulation. Holst *et al* (1963) concluded that the middle-ear muscle reflex is due to simultaneous contraction of both muscles. Terkildsen (1960) was more cautious and considered a definite action of the tensor muscle to be present on acoustic stimulation in only 62 % of the 60 human ears he examined. According to Mendelson (1966) the manometric direction of the reflex displacements of

series of tone burst for each frequency The system was calibrated in hearing level re: 1964 ISO standard reference. The tones were pre sented through a TDH 39 telephonic earphone and had a maximum hearing level of 120 dB However the maximum hearing level employed for most cases was limited to 110 dB.

Air-jet stimulation of the orbital region on the homolateral side of the recorded ear was performed according to Klockhoff & Anderson (1960). Tactile stimulation, according to Klock hoff (1961) and Djupesland (1964), was per formed with a twist of cotton wool on a stick in the homolateral concha and in front of the homolateral tragus, care being exercised to avoid touching the probe.

INTRA AURAL REFLEX RESPONSES

Responses on the amplitude balance meter A and on the amplitude and phase balance meter AP" and on the extratympanic manometer "P" were recorded simultaneously dur ing the presentation of stimuli.

According to Møller (1964) the middle-ear muscles act synergistically as far as impedance is concerned. That could imply an increase in the magnitude of the response in channel A when both muscles are contracting simultane ously However Figs 2 b and 2 c show the response to air-jet stimulation for two normal ears in which both muscles are assumed to be functioning, and yet the magnitude of the response is less than in Fig. 2 a, which represents *the response of an ear homolateral to supra*-stapedial facial palsy with only a functioning tensor muscle. This means that the reflex in dicator does not accurately measure the relative impedance change, but instead the change in SPL of the probe tone in the ear canal. Thus, the change of SPL in the ear canal does not appear to be proportional to change of impedance. Depending on the stimulus frequency and the resonance characteristics of the partic ular middle ear under study channel A" may show either negative or positive deflections.

The amplitude and phase of the probe tone are balanced to zero in the AC-bridge. Conse quently the deflections in this channel ("AP") are only positive.

The response P" indicates the movement of the tympanic membrane. This response is of special interest considering the fact that the tensor muscle presumably pulls the eardrum inward. As this movement occurs, the volume between the probe in the ear canal and the tympanic membrane will suddenly increase and the air pressure will decrease This situation will appear as a relatively large spike-like negative or downward deflection on the P" channel of the recorder An upward or positive deflection on the record indicates an outward movement of the eardrum. This response pat tern, unlike the negative downward deflection, is usually a slower shallow broader response and is considered to show stapedial muscle ac tivity We have also observed negative deflec tions of the same type, which we have inter preted as stapedial muscle contractions according to Mendelson s findings (1966) Therefore, whenever we observed a sudden spike-like negative deflection in the "P channel we always interpreted this pattern to show tensor muscle contraction. When the response was either neg ative or positive, but the pattern broad and shallow we interpreted this to show stapedial muscle contraction.

Subjects

Two groups of subjects were used for this investigation. One group was selected on the *basis of pathology* which presumably precludes a stapedial muscle reflex. The other group consisted of persons with normal hearing and otologically normal middle ears.

The pathological group contained the following subjects.

a. Supra-stapedial facial palsy with otologically-normal middle ears (N = 14)
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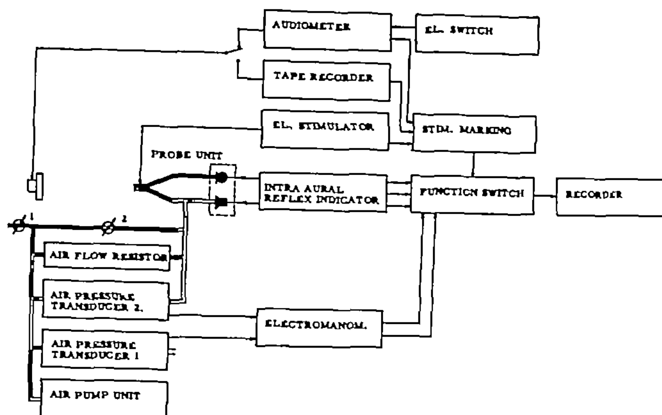


Fig. 1 Block diagram of the equipment.

a positive (upward) or negative (downward) direction. For the same purpose the *amplitude and phase* of the probe tone are balanced to zero in an AC bridge and connected to the third meter This bridge permits responses only in a positive (upward) direction. The capacity to balance *amplitude* as well as *amplitude and phase* was originally made in order to discover which of the two bridges offers the most easily interpreted responses. It should be mentioned that the two bridges provide responses of different magnitude The output from the second and third meters is recorded on the first two channels of a four-channel recorder (Mingograf type 34 Elema-Schönander)

Before the reflex measurements are made the middle-ear pressure is always checked by tympanometry The reason for this is that either abnormal positive or negative pressure may suppress the elicitation of the middle-ear reflexes The equipment and procedure for tympanometry is described in this issue (Lidén *et al* 1969)

Extratympanic manometry The change in air pressure produced by movements of the tympanic membrane is measured by a pressure transducer and electromanometer (Elema-Schönander Type EMT 32 and EM 31) and fed to the third channel of the recorder The highest sensitivity of the transducer corresponds to a change of ± 0.5 mm water pressure. In order to automatically balance the sensitive pressure transducer for changes in the static pressure in the ear canal an air flow resistor is provided with a time delay of 10 seconds.

Stimulation Pure tones corresponding to five different frequencies (250 500 1000 2000 and 4000 Hz) were recorded on magnetic tape with an intensity range of 40 dB in 2 5 dB discrete steps The on and off times were one and two seconds, respectively The rise and decay times were both 25 msec. The signals from the tape recorder were fed through an attenuator system which permitted the preselection of the maximum output for a given

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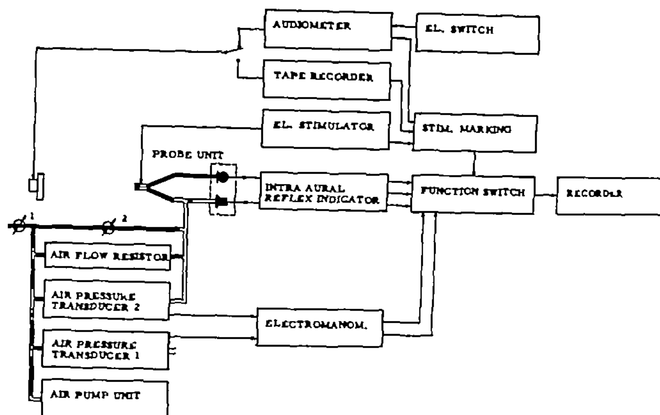


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The normal group consisted of 78 university students (127 ears) Each had a hearing threshold of 15 dB re ISO or better at test frequencies of 250 to 4000 Hz.

Procedure

All subjects were given an otological examination and a pure tone audiogram prior to the investigation of the middle-ear reflexes. Reflex responses during acoustic stimulation were conducted for all 78 normal subjects (127 ears) Air jet stimulation was performed on 59 of the normal subjects (93 ears) and tactile stimulation of the concha auriculi on 43 subjects (71 ears) Tactile stimulation of the tragus was conducted on 44 normal subjects (70 ears) All of the subjects in the pathological group were tested with acoustic stimulation Seventeen of the otosclerotic patients were tested by air jet and none by tactile simulation all of the patients with facial palsy were given air jet stimulation and none received tactile stimulation The reflexes were examined in these subjects by stimulation from tape-recorded pure tones, by an air jet directed towards the homolateral eye and by touching the skin of the homolateral choncha auriculae and on the tragus. In addition, a dual reflex pattern was recorded in seven of the normal subjects during simultaneous acoustic and air jet stimulation The stapedius muscle was brought into a state of maximum contraction by stimulating the non-recorded ear with a 1000 Hz pure tone, 30 dB above the pre-determined reflex threshold. During this sustained stimulation period of about 12 seconds, three air jet puffs were delivered towards the eye homolateral to the recorded ear For further comparison, the voluntary contraction of the middle-ear muscles was recorded in two of the normal subjects.

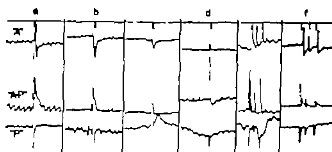


Fig. 2. Response patterns during air jet stimulation towards the homolateral eye. Paper speed 5 mm/sec.
a. Subject E B. 97 08 26. Unilateral supra-stapedial facial palsy right side Normal middle ear No response to acoustic stimulation. Probe in right ear
b. Responses from left, normal side in same subject as in Fig. 2 a. Normal responses elicited by acoustic stimulation. Probe in left ear
c. Subject I S. 44 04 10 Normal subject. Probe in right ear
d. Subject O. B 20 05 28. Stapes fixation, right ear Hearing level 47 dB No responses on acoustic stimulation. Left ear normal. Probe in right ear
e. Responses to three air jet from left stapedectomized ear same subject as in Fig. 2 d. No responses were obtained to acoustic stimulation.
f. Subject B. H 32 11 01 Stapedectomy right ear Left ear normal. Air jet repeated three times. No responses on acoustic stimulation Probe in right ear

RESULTS

Patients with Supra-stapedial Facial Palsy

None of the 14 patients with facial palsy showed any responses to acoustic stimulation Air jet stimulation towards the eye homolateral to the recorded ear however gave responses in 10 of the 14 patients. Figs. 2 a and 2 b show the response to air jet stimulation for the recording ear both ipsilateral and contralateral to the supra stapedial palsy in a 71 year-old man This pattern was similar for all 10 patients in this group who showed a response. For comparison, the responses to air jet stimulation in a subject from the normal-hearing group are shown in Fig 2 c.

Patients with Otosclerosis

None of the 25 patients with otosclerosis showed any activity of the middle-ear muscles upon acoustic stimulation. Seventeen of them were tested with an air jet stimulus directed towards the eye homolateral to the recording ear Nine patients had stapes fixation in the recording ear and eight had been stapedectomized.

Channels "A" and "AP" gave responses to air-jet stimulation in all 17 patients, and channel "P" in 15 patients. All the deflections in channel "P" were sharp negative spikes, thus suggesting tensor muscle contraction. As an example Fig. 2 d shows the response to air jet stimulation of the orbital region ipsilateral to the pre-operative otosclerotic ear in a 48-year-old female patient. Fig. 2 e shows the response to three air-jet puffs to the eye ipsilateral to the stapedectomized ear in the same patient. Fig. 2 f is a further example of the response to three repeated bursts of the air jet to the stapedectomized ear in a 36-year-old male patient.

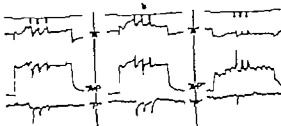


Fig. 3. Response patterns during combined stimulation with 1000 Hz tone, 115 dB HL for 12 sec. and volley of three air-jet puffs. Paper speed 5 mm/sec.
a. Subject E.B. 39 05 07. Normal subject. Probe in right ear
b. Same subject as in Fig. 3 a. Probe in left ear
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Normal Subjects

Combined Acoustic and Air Jet Stimulation

Reflex response patterns in seven normal subjects during the combined acoustic and air-jet stimulation were very consistent. The activity of the tensor muscle is superimposed on the reflex elicited by acoustic stimulation and is evident in all three channels. Figs. 3 a and 3 c represent selected examples of the results of this combined reflex pattern. Figs. 3 a and 3 b are the response pattern in a 29-year-old normal female. The recording on each channel of each figure readily displays the air-jet response superimposed on the response to acoustic stimulation. Fig. 3 c is a similar response pattern in a 28-year-old normal woman.

Voluntary Middle Ear Muscle Reflex

Two normal subjects could voluntarily contract their middle-ear muscles. Their reflex-response patterns were recorded and compared with the responses during air jet as well as combined acoustic and air-jet stimulation. Figs. 4 a, 4 b and 4 c illustrate these responses in a 51-year old man with normal hearing. Figs. 4 a and 4 b show what are presumed to be tensor muscle contractions as represented by the sudden, rapid spike pattern displayed. Fig. 4 c shows a single tensor muscle contraction resulting from air-jet stimulation superimposed on the response to acoustic stimulation. Unfortunately none of the subjects with non-functioning stapedial muscles could voluntarily contract the tensor muscle. Thus, we cannot exclude the possibility that responses during voluntary contraction also include a simultaneous stapedial muscle reflex. The general pattern, however is in favour of only a tensor contraction.

Acoustic Stimulation

Altogether data were collected for 127 ears of 78 normal-hearing subjects. The majority of the ears were stimulated with tones of five octave frequencies in the range from 250 Hz to 4000 Hz. In total, 640 frequencies were

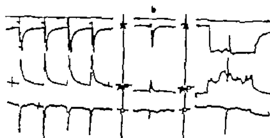


Fig. 4. Response patterns for subject H.H. 18 01 09. Paper speed 5 mm/sec.
a. Voluntary concentration for the middle-ear muscles. Probe in left ear
b. Air-jet stimulation. Probe in left ear
c. Combined stimulation with 1000 Hz tone, 15 dB above reflex threshold = 70 dB HL and air jet. Probe in left ear

The normal group consisted of 78 university students (127 ears) Each had a hearing threshold of 15 dB re ISO or better at test frequencies of 250 to 4000 Hz.

Procedure

All subjects were given an otological examination and a pure tone audiogram prior to the investigation of the middle-ear reflexes. Reflex responses during acoustic stimulation were conducted for all 78 normal subjects (127 ears) Air jet stimulation was performed on 59 of the normal subjects (93 ears) and tactile stimulation of the concha auriculi on 43 subjects (71 ears) Tactile stimulation of the tragus was conducted on 44 normal subjects (70 ears) All of the subjects in the pathological group were tested with acoustic stimulation Seventeen of the otosclerotic patients were tested by air jet and none by tactile simulation all of the patients with facial palsy were given air jet stimulation and none received tactile stimulation The reflexes were examined in these subjects by stimulation from tape recorded pure tones, by an air jet directed towards the homolateral eye and by touching the skin of the homolateral chончha auriculae and on the tragus In addition, a dual reflex pattern was recorded in seven of the normal subjects during simultaneous acoustic and air jet stimulation. The stapedius muscle was brought into a state of maximum contraction by stimulating the non-recorded ear with a 1000 Hz pure tone 30 dB above the pre-determined reflex threshold During this sustained stimulation period of about 12 seconds, three air jet puffs were delivered towards the eye homolateral to the recorded ear For further comparison, the voluntary contraction of the middle-ear muscles was recorded in two of the normal subjects.

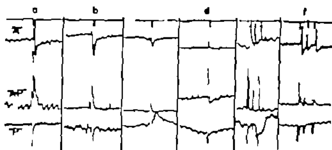


Fig. 2. Response patterns during air jet stimulation towards the homolateral eye. Paper speed 5 mm/sec.
a. Subject E. B. 97 08 26. Unilateral supra-stapedial facial palsy right side Normal middle ear No response to acoustic stimulation. Probe in right ear
b. Responses from left, normal side in same subject as in Fig. 2 a. Normal responses elicited by acoustic stimulation. Probe in left ear
c. Subject I S 44 04 10 Normal subject. Probe in right ear
d. Subject O B 20 05 8. Stapes fixation, right ear Hearing level 47 dB No responses on acoustic stimulation. Left ear normal Probe in right ear
e. Responses to three air jet from left stapedectomized ear same subject as in Fig. 2 d. No responses were obtained to acoustic stimulation.
f. Subject B H 32 11 01 Stapedectomy right ear Left ear normal. Air jet repeated three times. No responses on acoustic stimulation Probe in right ear

RESULTS

Patients with Supra-stapedial Facial Palsy

None of the 14 patients with facial palsy showed any responses to acoustic stimulation. Air jet stimulation towards the eye homolateral to the recorded ear however gave responses in 10 of the 14 patients. Figs. 2 a and 2 b show the response to air jet stimulation for the recording ear both ipsilateral and contralateral to the supra-stapedial palsy in a 71 year-old man This pattern was similar for all 10 patients in this group who showed a response For comparison, the responses to air jet stimulation in a subject from the normal-hearing group are shown in Fig 2 c.

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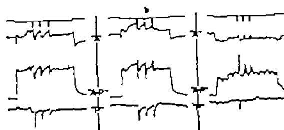


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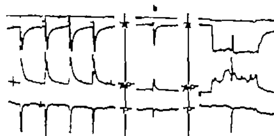


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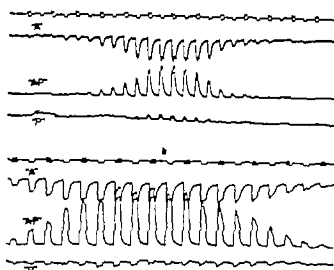


Fig. 5 Response patterns in normal subjects during acoustic stimulation Paper speed 5 mm/sec.
a. Subject J J 43 10 17 2000 Hz, 80–110–80 dB HL. Probe in right ear The positive deflections in channel P are interpreted as stapedial reflexes.
b Subject G S 43 03 16. 4000 Hz 75–105–75 dB HL. Probe in right ear The negative shallow deflections in channel P are interpreted as stapedial reflexes.

used for stimulation in the 78 subjects. In 80 % of the frequencies, a maximum HL of 110 dB was used, and in 20 % 120 dB HL was used

All of the 127 ears gave clear responses on channels "A" and "AP" On channel P" on the other hand, responses were recorded for only 44 % of all frequencies tested A positive deflection, as shown for example in Fig. 5 a, was noted in 26 % of all tested frequencies. Translated to percentages of subjects, the results show that 51 % of the 78 subjects had responses with positive deflection at some of the frequencies tested. It should be remembered that a positive deflection in channel "P is interpreted as a stapedial muscle response (S+)

In 14 % of all tested frequencies, or in 30 % of the subjects, a shallow broad negative deflection was found for some of the frequencies (Fig 5 b) Since these responses do not show the sharp spike like negative pattern, they were interpreted as the result of stapedial muscle contraction (S−)

A very large negative deflection *increasing with intensity* of the acoustic stimulation was used as a criterion for a tensor muscle response (T) In 10 of the 78 subjects, or nearly 13 % such a response was observed (Figs. 6 a, 6 b and 6 c) However calculated on the basis of all tested frequencies there was evidence of

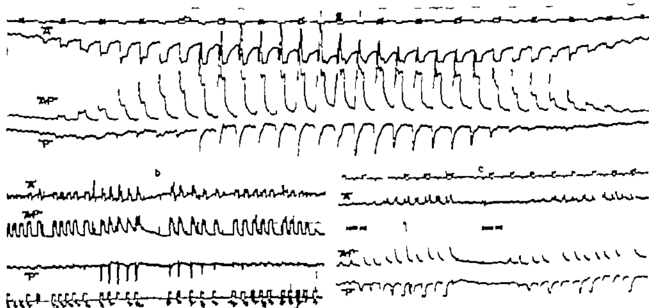


Fig. 6. Response patterns in normal subjects during acoustic stimulation The sharp spike like negative deflections in channel P" are interpreted as tensor reflexes.
a. Subject L.B N 49 04 12. 500 Hz 80–120–80 dB HL. Probe in left ear
b. Subject K.B. 42 03 25 500 Hz 90–120–90 dB HL. Probe in right ear
c. Subject T.E. 44 07 20 1000 Hz 75–105 dB HL and 000 Hz, 70–105 dB HL. Probe in left ear

Table 1 *Response in per cent during air-jet and tactile stimulation for normal subjects in channels A AP" and "P"*

	N (ears)	Channel A		Channel AP"		Channel "P"			
		R	NR	R	NR	–	+	B	NR
Air jet	93	97	3	94	6	59	9	13	19
Concha	71	84	16	83	17	34	11	4	51
Tragus	70	48	52	46	54	45	7	3	45

Abbreviations:
R = response.
NR = no response.
– = neg. deflection.
+ = positive deflection
B = biphasic response.

tensor activity in only 4 % of the measurements. An isolated negative or spontaneous response which could not be repeated was disregarded.

Air Jet and Tactile Stimulation

Recordings during air jet stimulation directed towards the homolateral eye were obtained on 93 normal ears. The concha auriculae and tragus of 71 and 70 ears, respectively were touched with a twist of cotton wool attached to an applicator The results are shown in Table 1 Stimulation of the concha seems, according to this investigation, to give better responses than on the tragus.

COMMENTS

The reflex pattern in channel "P" indicating induced movement of the tympanic membrane, was used primarily to identify the activity of the tensor muscle Sharp, spike-like negative deflections, increasing with the intensity of the acoustic stimulus, were interpreted as tensor contractions. A change in the reflex pattern of channels A and AP" simultaneously with the appearance of these spike-like deflections lend additional support to this assumption. The identification was also based on investigations of reflex patterns in the subjects in whom the tensor was the only functioning muscle in the middle ear Likewise, the reflex patterns during the combined acoustic and air jet stimulation as well as during the voluntary contraction of the middle ear muscles, contribute to a clearer recognition of the tensor response The tensor reflex, identified by a negative deflection which increases in magnitude with an increase in the intensity of acoustic stimulation, was found in only 13 % of our normal-hearing subjects. About half of these tensor responses appeared first at levels above 110 dB HL. However nearly as many appeared starting at about 100 dB HL.

The tensor reflex during air-jet stimulation has been considered to be part of a startle reaction. Strong squinting of the eyes or contraction of the muscles of the face may elicit the tensor reflex. For this reason, the subjects were observed closely during the period of acoustic stimulation. None of the subjects with apparent tensor responses gave evidence of intolerance or reacted with facial muscle contractions. Thus, we feel it is justified to consider the recorded response in this minority group of normal subjects as an acoustic tensor reflex. In the group with pathological middle ears in which the tensor muscle was the only functioning muscle the tensor reflex could not be elicited by acoustic stimulation for any subject. Tables 2 and 3 summarize the results of acoustic and air-jet stimulation.

Table 2 *Impedance and extratympanic manometry responses in per cent during acoustic and air jet stimulation for all subjects*

	Pure tones Channels				Air Jet Channels			
	N	A	"AP"	P"	N	A	AP"	P"
Facial palsy	14	0	0	0	14	70	70	70
Stapes fixation	13	0	0	0	9	100	100	90
Stapedectomy	1	0	0	0	8	100	100	90
Normal subjects	78	100	100	8	59	97	94	81
Number of frequencies	640	100	100	44				

CONCLUSIONS

Simultaneous recording of changes in relative impedance and air pressure give a more complete picture of the behaviour of the middle-ear muscle reflexes. *By this method it is easier to* identify the response of the tensor muscle.

Extratympanic manometry may provide interesting supplementary information However in our opinion this technique is not necessary for diagnostic purposes. In our judgement, response patterns on the reflex indicator and on the manometer during acoustic stimulation are primarily due to the stapedial muscle reflex, i.e these responses can be observed on a reflex indicator without the aid of a manometer

In a small fraction of the group of normal subjects (13 %) the recording patterns suggest that both muscles contract during acoustic stimulation. The stapedial muscle appears to have a reflex threshold at a lower sound pressure level than the tensor muscle

ACKNOWLEDGEMENT

This study has been supported, in part, by the Swedish Medical Research Council B69-17X 133-03A and, in part by a Public Health Service Fellowship 1 F03 HD-39 671-01 from the National Institutes of Health. Dr Peterson is a National Institutes of Health Special Research Fellow on leave of absence from Louisiana State University School of Medicine

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Table 3 *Response in per cent during acoustic stimulation by extratympanic manometry (Channel "P") in all normal subjects*

	S+	S	T
Per cent of tested frequencies (N = 640)	6	14	4
Per cent of number of subjects (N = 78)	51	30	13

in the tensor tympani muscle recorded in man. *Acta Otolaryng* (Stockh.) *51* 184.

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DISCUSSION

K. Terkildsen. I do not understand why contraction of the tensor muscle can cause a reduction in the tympanic membrane impedance. These "negative" reflexes come with a very short latency and the mechanism of this type of response must still be kept under discussion.

Neergaard. It should be noted in connection with the evaluation of pressure changes in the ear canal that an inward displacement of a curved membrane may well give rise to a volume displacement in the opposite direction. So a recording of volume displacements or pressures is not sufficient for the assessment of the movements of the central part of the membrane.

G. Lidén (Reply to Terkildsen). The middle ear muscles act synergistically as far as impedance is concerned. The reflex indicator, however, does not accurately measure the relative impedance change, but instead the change in SPL of the probe tone in the ear canal. Thus, a simultaneous contraction of both middle-ear muscles behaves antagonistically as far as measurement of a change in SPL is concerned, reducing the magnitude of the response.

(Reply to Neergaard). You are right. As I mentioned, Mendelson (1966) pointed out the same thing.

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TYMPANOMETRY

A METHOD FOR ANALYSIS OF MIDDLE EAR FUNCTION

G Lidén, J L. Peterson and G Björkman

From the Department of Audiology Sahlgren s Hospital Göteborg and Louisiana State University School of Medicine New Orleans, Louisiana U S A

Tympanometry is a method for evaluation of the mobility of the ear drum and the functional condition of the middle ear This is performed by measuring the ability of the tympanic membrane to reflect a probe tone in response to gradually changing air pressure in the ear canal. Four tympanometric characteristics were measured in a series of 100 normal ears. These results were compared with those obtained in patients with different types of conductive pathology The observed patterns in these patients with different audiological diagnoses were confirmed by surgery and by comparison with a series of fresh human temporal bones in which discrete lesions were created.

Tympanometry is a technique used to assess the mobility and the condition of the tympanic membrane and the middle ear during variation of the air pressure in the ear canal (Andersson *et al* 1956 Terkildsen & Thomsen 1959 Klockhoff 1961 Lidén & Nordlund, 1962 Hallén *et al* 1964 Lidén, 1969 a, 1969 b)

Tympanometry has been used as a routine clinical test in the Audiology Department, Sahlgren s Hospital, Göteborg since 1961 The purpose of this study was to evaluate systematically particular tympanometric characteristics for stability of response in normal ears compare these results with those obtained for various pathological conditions and assess such differences as an aid to diagnosis.

Subjects

A series of 100 otologically normal ears from subjects with a mean age of 27 years was studied to provide baseline data. The conductive group composed of 28 subjects with a mean age of 41 years, had various pathological middle-ear lesions, i. e. otosclerosis, secretory otitis media, chronic adhesive otitis media and disruption of the ossicular chain. A sensorineural group with a mean age of 47 years consisted of 20 subjects and was included in the investigation for comparison purposes.

Equipment

The basic instrument for tympanometry is the intra aural reflex indicator with probe unit described by Lidén *et al* (1969 a, 1969 b) A simplified block diagram is shown in Fig. 1 An 800 Hz probe tone is generated by the oscillator circuit of the reflex indicator and routed to a hearing aid type receiver mounted in the housing at the end of the probe unit. This signal is directed through one channel of the probe which is sealed by a foam-plastic cuff in the external auditory canal The pick up microphone in the probe unit monitors the sound pressure level in the ear canal between the tympanic membrane and the cuff of the probe The SPL of the probe tone is displayed on a meter of the reflex indicator The air pump unit creates a continually changing air pressure in the ear canal from −200 mm water to +200 mm water over 45 seconds. This change in air pressure is monitored by a pressure transducer and electromanometer (Elema-Schönander type EMT 34 and EM 31) The tympanogram i e the reflection of the probe tone indicates the change of impedance of the tympanic membrane due to the induced air pressure load The probe tone is adjusted to 70

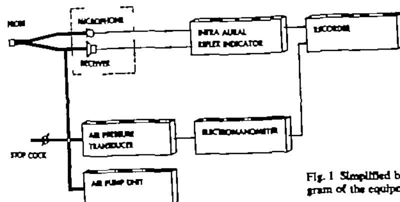


Fig. 1 Simplified block diagram of the equipment.

dB SPL at the starting point of −200 mm water The tympanogram with its corresponding air-pressure load is simultaneously displayed on a Mingograf recorder

Procedure

All subjects had an otological examination and hearing tested by pure-tone audiometry Speech audiometry was also performed for all subjects in the conductive and sensorineural groups. Tympanometric curves were then obtained.

Three subjects in the normal group were selected for a reliability study of the tympanometric curve Twenty tympanograms were obtained for the experimental ear of each subject over a 10-hour period.

The four measured tympanometric characteristics are illustrated in Fig. 2 for a 25-year old female with normal hearing and a normal tympanic membrane and middle ear The V shaped curve shows the tympanogram. The diagonal line is a recording of the air pressure change from −200 mm to +200 mm water The first characteristic is the "V" or notch, which is measured in dB

The second characteristic is the position of the notch relative to zero air pressure. The third characteristic is the width of the notch. It is found by determining half the maximum depth of the notch in dB and projecting this point to the intersection with the negative and positive halves of the tympanogram. These points are then projected to the diagonal pressure line where the width is measured in mm water The fourth characteristic measured in defining the tympanogram is the difference in SPL between the two end points of the tympanogram (upper right, Fig. 2)

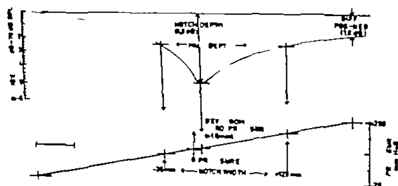


Fig. 2. Tympanometric characteristics for a 25-year old woman with normal hearing, normal tympanic membrane and middle ear The V-shaped curve shows the tympanogram. The diagonal line is recording of the air pressure change from −200 mm to +200 mm water

Table 1 *Means and standard deviations of tympanometric characteristics for subjects in the normal group otosclerotic ears in the conductive group and the sensorineural group*

Ears		Depth (dB)	Width (mm) Neg.	Width (mm) Pos.	Dev 0 (mm)	Diff (dB)
Normal	X̄	5.3	−29 7	+95 4	+10.0	1 6
N = 100	SD	±2.0	±20.0	±46.6	±15 0	±0._
Otoscler	X̄	5 4	−38.8	+92.6	+ 3.3	1.5
N = 29	SD	±2.0	±30 1	±50 0	±27.3	±0.6
Sen. neur	X̄	4 8	−45 4	+96.5	+ 2.8	1.3
N = 27	SD	±1 7	±25 1	±58 4	±26.1	±0.1

RESULTS

Means and standard deviations for all normal ears, those with otosclerosis from the conductive group and all subjects in the sensorineural group are shown in Table 1 The four measured characteristics of notch depth notch width, deviation from atmospheric pressure for the notch and the difference in SPL between maximum and minimum air pressures are approximately the same in all three groups. This observation was supported by a statistical analysis, which showed no significant difference among the groups Fig. 3 illustrates the mean curves for the three groups This comparison shows a highly similar pattern to the curves for each group

The results for three normal subjects selected for the reliability study did not show any statistical difference either when within-subject comparison were made (Table 2) These results indicate good stability for tympanometric configuration when a subject serves as his own control The standard deviations for the normal group (Table 1) also show little spread around the obtained means, indicating good between-subject stability as well. Fig. 4 illustrates the first, fifth, tenth fifteenth, and twentieth tympanograms for subject 1 obtained over the 10-hour test period Similar internal relationships were observed for subjects 2 and 3

Tympanograms obtained for those subjects in the conductive group with sequelae of various types of otitis media and disruptions of the ossicular chain were different in many respects. Fig 5 A shows the tympanogram of the right ear for a 63 year-old man with a large thin scar in the posterior half of the tympanic membrane after recurrent otitis media. The hearing tests gave no support to diagnosis of disruption of the ossicular chain. The two sharp distinct peaks ("W" pattern) near zero air pressure represent the points of treatest tympanic membrane mobility The tympanogram for the left

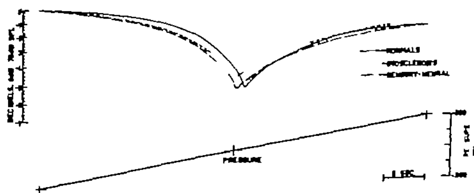


Fig. 3 Mean tympanometric curves for 100 normal ears, 9 otosclerotic ears and 27 sensorineural ears.

Table 2. *Means and standard deviations of tympanometric characteristics for three normal subjects each tested 20 times*

Subject		Depth (dB)	Width (mm)		Dev 0 (mm)	Diff. (dB)
			Neg.	Pos.		
1	$\bar{X}$	4.6	−33.8	+82.5	+4.8	1.0
	SD	±0.3	±7.4	±9.4	±6.2	±0.1
2	$\bar{X}$	3.6	−17.2	+103.5	+11.8	1.1
	SD	±0.2	±7.2	±15.0	±8.8	±0.4
3	$\bar{X}$	10.3	−25.0	+55.0	+2.5	1.4
	SD	±0.4	±8.3	±7.6	±7.2	±0.1

ear (not shown) resulted in a flat straight line caused by a perforation.

Fig 5 B shows the tympanogram for the left ear of a 9-year-old boy with recurrent colds. Otoscopic examination revealed a retracted membrane. The tympanogram shows a dramatic shift of the notch to approximately −200 mm water resulting from an abnormal negative air pressure in his middle ear

Fig. 5 C shows the tympanogram for a 10-year-old boy with a history of conductive hearing loss and serous otitis media, bilaterally. Otoscopic examination showed a retracted left tympanic membrane with effusion in the middle ear. The right tympanic membrane was normal, but effusion was also present in this middle ear. The tympanograms for both ears are similar showing an extremely flat, saucer-shaped curve. Only the curve for the right ear is illustrated.

Disruption of the ossicular chain will also produce an abnormal tympanogram. Fig. 5 D shows such a curve for a 66-year-old man with a history of chronic otitis media. Otoscopically the right ear showed a large atrophic scar in the posterior superior quadrant with abnormally high mobility when evaluated with the Siegle loupe and pressure bulb. Audiologically erosion of the long process of the incus was suspected and was later confirmed at operation. The tympanogram showed a highly irregular pattern across the entire air-pressure range. The tympanic membrane scarring plus erosion of the long process of the incus are undoubtedly the causal factors for the unusual shape of this curve.

The tympanogram for the right ear of a 38-year-old woman who had been operated on for otosclerosis is illustrated in Fig. 5 E. Stapediolysis had been performed on this ear in 1966. Otoscopy in the present examination, revealed a small atrophic scar in the upper posterior quadrant. The hearing had returned to near the pre-operative level. Based upon the

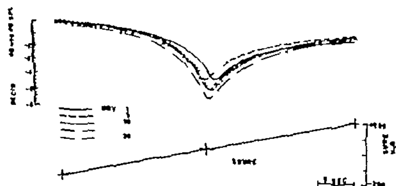


Fig. 4. Test-retest comparison of five tympanograms for subject 1 obtained over a 10-hour period.

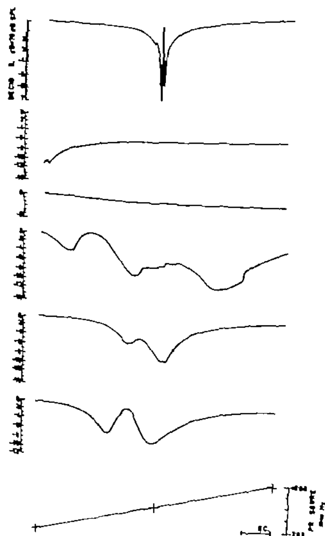


Fig. 5 Abnormal tympanometric curves.

A. Right ear tympanogram for a 63-year-old man with a large thin scar in the posterior half of the tympanic membrane and a history of recurrent otitis media.

B Left ear tympanogram for a 9-year-old boy with recurrent colds and a severely retracted tympanic membrane indicating abnormal negative pressure in his middle ear

C. Right ear tympanogram for a 10-year-old boy with a history of conductive hearing loss and bilateral serous otitis media with effusion in the middle ear

D Right ear tympanogram for a 66-year-old man with a history of chronic otitis media and a large atrophic scar in the posterior superior quadrant of the tympanic membrane and abnormally high mobility of the ear drum as evaluated with the Siegle loupe. Erosion of the long process of the incus was suspected and later confirmed at operation.

E. Right ear tympanogram for a 38-year-old otosclerotic woman on whom stapediolysis had been performed in 1966. At the present examination a small atrophic scar was found in the upper posterior quadrant. Fracture of both crura was also suspected at this time and later confirmed during stapedectomy surgery

F Left ear tympanogram for a 22 year-old man on whom stapedectomy had been performed for otosclerosis. Otoscopy revealed a normal-appearing, but hypermobile tympanic membrane.

tympanogram, fracture of both crura was suspected. This was confirmed during subsequent surgery The tympanogram shows a large broad undulating peak to the negative side of atmospheric pressure.

Fig 5 F shows the post-operative tympanogram for the left ear of a 22 year-old man with otosclerosis upon whom a stapedectomy procedure had been performed. The pre-operative curve (not shown) was quite normal. The post operative curve obtained 3 months after surgery shows a peak similar to that in Fig. 5 E deflected to the negative side of zero air pressure Postoperative otoscopy showed a super mobile tympanic membrane. Many stapedectomized ears have less than normal mobility The tympanograms in these postoperative otosclerotic ears have normal shape with the prostheses in place More often, however an abnormal tympanogram is found in a post operative otosclerotic ear The exact shape of it will vary in detail but the basic pattern will be similar to that shown in Fig. 5 F

DISCUSSION

Tympanometry provides a method of evaluating tympanic membrane mobility the air cushion of the middle ear and the integrity of the ossicular chain and associated structures. It provides clinically useful information which can be obtained by no other currently available test.

A normal tympanic membrane and middle ear will show a smooth, notched curve over an air-pressure range from −200 to +200 mm water with the notch occurring near atmospheric pressure Measurement of the four tym

panometric characteristics will closely approximate the data presented in Table 1 for the 100 normal ears when 800 cps is used as the probe frequency

In otosclerosis where no pathology other than stapes fixation is present the normal configuration of the tympanogram is not distorted The same is true for all patients with sensorineural lesions.

Several distinctive tympanometric curves can be identified as related to specific pathological conditions:

1 Flat, straight-line pattern. This curve will be found in ears which show a tympanic membrane perforation, a serous otitis media or chronic adhesive otitis media. The tympanic membrane is unresponsive to the applied air pressure either because of the perforation or because the tympanic cavity is filled with fluid, exudate or adhesions.
2. Rapid, oscillatory patterns near pressure balance point ("W" pattern) This shape will be seen frequently in patients with tympanic membrane scarring.
3 Large, broad undulating peaks: Curves of this kind can be observed in patients with disruptions of the ossicular chain. This pattern has also been seen in otosclerotic patients who have undergone stapedectomy
4 Tympanometric pressure-balance point deviated to the negative side of atmospheric pressure indicating negative middle-ear pressure This pattern is seen in impaired Eustachian-tube function. The extent to which the notch is shifted can show a relationship to elevated reflex thresholds or air bone gap seen in pure-tone audiometry (Peterson et al.).

A slight deviation of the notch to positive pressure does not seem to be a pathological sign, but evidence of good tubal function. In fact, the normal group showed a deviation corresponding to +10 mm water (Table 1). The otosclerotic and sensorineural groups both showed a positive pressure in the middle ear corresponding to +3 mm water The standard deviation in the normal group was ±15 mm and about ±27 mm in the pathological groups. Furthermore, reversing the ear-canal air-pressure change, to run the test from plus to minus 200 mm water does not alter the results. This minor deviation of the notch from atmospheric pressure is presumably due to a hysteresis effect of the impedance of the tympanic membrane resulting from the applied pressures. Thus, a minor residual positive pressure shown by tympanometry is presumed to indicate normal tympanic membrane behaviour and tubal function.

The above four patterns represent the basic shapes that have been observed. Minor variations will be seen in the patients, but significant departures from these patterns would not be expected. It is our experience that frequently a combination of abnormal conditions will be present resulting in a tympanogram not typical of any of the above patterns.

In order to identify the tympanometric effect of pure lesions, a series of fresh human temporal bones was studied by Peterson & Lidén (1969) Discrete experimental lesions were created in the middle ears of the bones and tympanometric shape observed. For example fracturing the crura or separating the joint between the malleus and incus or between the incus and stapes produced tympanograms similar to those shown in Figs. 5 D–F Filling the middle ear with water resulted in a tympanogram similar to that seen in Fig. 5 C. A negative or positive pressure applied to the middle ear of these bones shifted the notch to the left or to the right to a point at which the air pressures on both sides of the ear drum corresponded. These results have permitted interpretation of tympanograms in living ears with greater assurance.

Tympanometry is of significant clinical value A pathological shape to the tympanogram when it is not expected alerts the surgeon and will permit him to judge the potential success of the planned operation. For this reason, as well as others illustrated above, tympanometry has become a routine diagnostic test for all

cases with middle-ear lesions seen in our department.

ACKNOWLEDGMENT

This study was supported, in part, by the Swedish Medical Research Council B69 17X 133-03A and in part, by a Public Health Service Fellowship 1 F03 HD-39 671-01 from the National Institutes of Health. Dr Peterson is a National Institutes of Health Special Research Fellow on leave of absence from Louisiana State University School of Medicine.

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REVERSE FREQUENCY SWEEP BÉKÉSY AUDIOMETRY

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A Grason-Stadler E800 Békésy audiometer was used for threshold measurements with sweep-frequency technique starting from the low tones (forward) and then from the high frequencies (reverse). The tracings were superimposed for both interrupted and continuous tones in normal-hearing subjects and in cochlear deafness. In some cases, most frequently in retrocochlear lesions, the reverse tracing was poorer than the forward curve for continuous tones in the middle and/or high-frequency regions. This behaviour was associated with pronounced threshold tone decay and, almost without any exceptions, with negative or incomplete recruitment.

In Békésy audiometry the conventional threshold measurements are carried out with interrupted and/or continuous stimuli starting from low tones. On the basis of these tracings, Jerger (1960) and Jerger *et al.* (1962) described four separate types: in normal hearing continuous and interrupted tone tracings overlap (type I) in cochlear deafness the continuous tone tracings may be poorer at the high frequencies (type II) the separation may be very pronounced in the middle and high range (type III) or it occurs at all frequencies (type IV). Type III is often associated with retrocochlear deafness. Corso & Wilson (1951) utilized a reverse frequency sweep in testing 10 normally hearing subjects. With continuous and interrupted stimuli the thresholds for high frequencies were found to be better with the forward sweep than with the reverse sweep; the opposite was the case at the low frequencies. In Epstein's (1960) 15 subjects with sensorineural deafness the thresholds tested in the range 200–4000 cps were poorer at 3000 cps with the forward sweeping than when the reverse order was used.

The measurements of Rose (1962) in 47 patients with perceptive deafness were made with pulsed and continuous tones between 100 and 10 000 cps using the attenuation rate of 2.5 dB/sec. In mild hearing loss (20 dB or less) the thresholds were generally not affected. His case histories, including both cochlear and retrocochlear lesions, suggested that the reverse frequency sweep gives poorer thresholds in high- or middle-frequency regions. In some cases, when the conventional forward method did not reveal an interrupted-continuous tone gap such a gap was demonstrated with the reverse frequency sweeps.

TESTING TECHNIQUE AND MATERIAL

The apparatus used was a Grason-Stadler Model E 800 Békésy audiometer operating at SPL with a 0.0002 dyn/cm² zero-level at all frequencies. The test subject was instructed to press the switch immediately a tone was heard and to release it as soon as the tone disappeared. With an attenuation rate of 4.2 dB/sec., the sweep over the frequency region 125–8000 cps took 3¹/₃ min. The testing was started from the low tones, the reverse frequency sweep following after a pause of a few seconds. Tests were made with interrupted and continuous tones; the former consisted of 200 msec pulses with a rise and fall time of 25 msec, presented at intervals of similar length.

cases with middle-ear lesions seen in our de partment.

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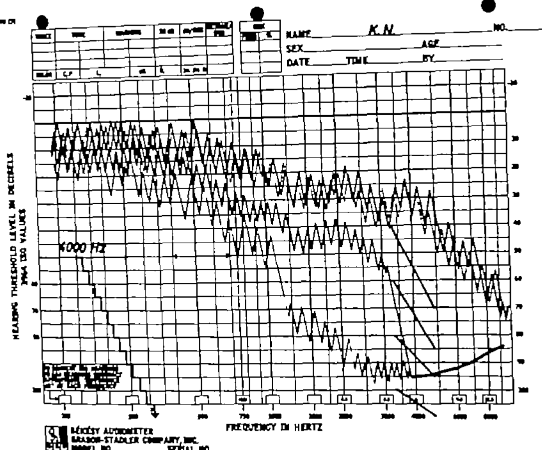


Fig. 1 Békésy tracings registered by two-octave technique for the affected frequencies 2000–8000 cps in a patient with hypertension and angiosclerotic cerebral disorder. The overlapping upper pair of curves are the forward and reverse tracings with interrupted test tone. The continuous tone tracings lie definitely apart: the forward curve (middle) is clearly better than the reverse (bottom). Threshold tone decay test shows total disappearance of test tone at 4000 cps in 90 sec. there is incomplete recruitment at 4000 cps.

Although the poor reverse threshold was accompanied with pronounced threshold tone decay the latter could appear in association with a normal reverse sweep. Thirty-one ears with threshold tone decay of 30 dB or more (in two cases over 60 dB) showed overlapping tracings, in 20 cases recruitment was complete, in five ears absent, and in six cases incomplete.

Compared with Jerger's classification, abnormally poor reverse tracings occurred among all four types, two cases even representing type I. A similar distribution is seen in the cases reported by Rose. It seems that abnormal adaptation is the most likely explanation for the separation of the tracings, even if the exact mechanism is obscure. It is known that post stimulatory threshold shift after low-intensity exposure is nearly symmetrical around the stimulus frequency. It has, however, a tendency to spread towards the high frequencies. After high intensity stimulation, the maximum threshold shift occurs half an octave above the stimulating frequency. Thus, the forward continuous-tone sweep might be expected to give poorer threshold values than the reverse test, indeed, Epstein (1960) and Harbert & Young (1962) reported such results. In agreement with Rose's results (1966) we were unable to con-

Table 1 *Results in patients with sensorineural hearing loss*

Diagnosis	Patients	Ears	Abnormal tracings
Ménière s disease	38	38	1
Acoustic trauma	16	23	1
Noise injury	30	47	
Streptomycin damage	6	8	
Postinfectious deafness	8	8	
Vestibular neuronitis	4	4	
Vascular accident	9	9	1
Angiosclerotic degeneration	24	37	2
Head injuries	25	31	6
Presbyacusis	16	2[illegible]	
Hereditary or congenital deafness	18	26	1
Infratentorial tumour	[illegible]	2	2
Supratentorial tumour	1	1	
Diffuse central lesion	10	12	1
Functional hearing loss	2	2	1
Undetermined sensori neural deafness	12	14	1
Total	221	284	17

If there was any abnormality between tracings, control measurements were made in the af fected area with the two-octave frequency sweep technique Preliminary measurements were made on both ears of three experienced observers and on one ear of 10 normally hear ing inexperienced listeners (Palva *et al* 1969) The series consisted of 221 patients with sensorineural hearing loss the number of tested ears totalled 284 In addition to air and bone conduction conventional threshold measure ments, speech audiometry recruitment testing by Fowler s or Reger's method and the thresh old tone decay test were employed.

RESULTS

The results in the patients with sensorineural hearing loss are presented in Table 1 In 17 of the 221 patients there was a separation of the continuous tone tracings exceeding 10 dB and it was always the reverse frequency sweep that gave poorer threshold values than the for ward testing order The separation appeared most often at the high and middle frequencies, occasionally also at low tones. It was always accompanied with a pronounced threshold tone decay (30–60 dB in 3 minutes, the test tone often disappearing totally) and with in complete or negative recruitment (exceptions were one patient with Ménière s disease and another with acoustic trauma) The amount of separation was in most cases 30–50 dB The forward and reverse tracings with interrupted test tones were superimposed in each of the cases studied

The patients with separated reverse tracings included two with severe angiosclerotic disease. Two patients had an infratentorial brain-base tumour and one patient a diffuse central le sion resulting from meningo-encephalitis. In a subgroup of 25 patients with head injuries, abnormal tracings were observed in six. They had all sustained severe injury with cerebral contusion A vertebral artery occlusion was found in one case of vascular accident. A separation between the forward and reverse sweeps was observed in only two cases of pure cochlear lesion In one, the patient suffered from Ménière s disease and medication had proved ineffective but attacks were later re lieved after decompression of the endolymphatic sac the other patient had an old acoustic trauma with troublesome tinnitus.

Fig. 1 shows a typical result obtained by testing the affected frequencies with the two-octave technique. The patient suffered from hypertension with angiosclerotic degeneration. She was under examination because of vestibular symptoms

DISCUSSION

In this series of perceptively deaf ears the abnormal separation of the forward and reverse Békésy tracings was always accompanied with pronounced threshold tone decay and gener ally with negative or incomplete loudness re cruitment. Accordingly the abnormally poor reverse tracings were as a rule associated with retrocochlear lesions (Table 1) and only twice with a pure cochlear lesion with complete re cruitment.

Acta Otolaryng. 263 229–230, 1970

AUDIO-VISUAL SPEECH PERCEPTION

A PRELIMINARY REPORT

H. W Ewertsen, H. Birk Nielsen and S. Scott Nielsen

From the Stat Hearing Rehabilitation Centre Bispebjerg Hospital, Copenhagen, Denmark

By means of a video-recorder connected to a speech audiometer and television set it is possible to vary independently the two parameters, the picture and the sound level. The communication score of 100 persons as found in relation either to the visual perception alone or to the auditive perception and, finally to combination of both. In the group of patients with medium lipreading ability there seems to be fairly good correlation between this ability and the reduction of their hearing loss measured in decibels. A small group seems to have special capacity of combining vision and hearing

It is a well-known fact that vision can, to a variable extent, substitute failing audition. The easiest words to lipread are numbers, because the possibilities of guessing are few but the ability of various people to lipread other words varies in correctness from 0 to 100 %

During the last few years we have tried objectively to evaluate the lipreading ability of our patients by exposing them to a silent colour film of about three minutes duration representing the familiar situation of two people having coffee together and saying nine sentences in all.

Two years ago we bought a video-recorder (Philips). This is a kind of tape-recorder by means of which a picture and the connecting speech can be reproduced on a TV set, on which the intensity of the speech can be adjusted in decibel steps through the audiometer By means of this equipment it is possible independently to vary the two parameters—the visual and the auditive perception.

We had some discussion regarding the selection of speech material and how to quantify the performance of the patient. Should he repeat every single word in each sentence, or was it satisfactory if he perceived the meaning of the sentence? After some introductory experiments, we began to use short sentences giving instructions to the patients, such as: Rub your nose "Cross your arms" Lift your foot" etc. It was then recorded whether or not the patient actually did as he was told. This procedure was approved by our test psychologist Jan Ratleff

The patients are tested in three situations:

1 *Hearing Alone*

We start with five sentences presented 10 dB below the patient's speech-reception threshold, and then five sentences at the threshold, five sentences 10 dB above threshold, five sentences 20 dB above threshold, five sentences 30 dB above threshold.

2. *Vision Alone*

The same 25 sentences, but in a different se

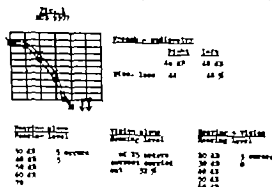


Fig. 1 Audiogram of a patient with high-tone loss. The speech-reception threshold is 40 dB in either ear At each of the indicated hearing levels five sentences (orders) are given, and the number of errors is stated.

firm these findings in any case Control runs were also carried out the sweep was started at the high frequencies and the forward frequency sweep followed next. However the results in abnormal cases were the same as in the conventional order of frequency testing neither did the results differ from one another in overlapping cases.

The forward and reverse frequency sweeps seem to give more information than conventional Békésy audiometry Our results indicate that abnormal results are obtained in a certain number of those cases of hearing impairment that show great fatigability or much adaptation. It remains to be seen whether with added experience, a definite diagnostic value can be assigned to this interesting phenomenon.

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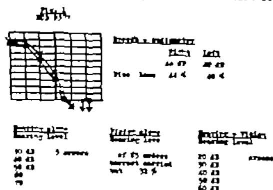


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CLICK-EVOKED RESPONSES IN THE MEDIAL GENICULATE BODY IN AWAKE CATS

B. Etholm, L. Olsen and K. Skrede

From the Institute of Neurophysiology University of Oslo, Norway

A method for recording from the medial geniculate body in awake cats is reported. The pattern of the response was similar to that seen in anaesthetized cats. By using double clicks, there was depression f excitability following an excitatory response which lasted only 20–30 msec. Giving the animal barbiturate anaesthesia (30 mg/kg), the inhibitory period was greatly prolonged.

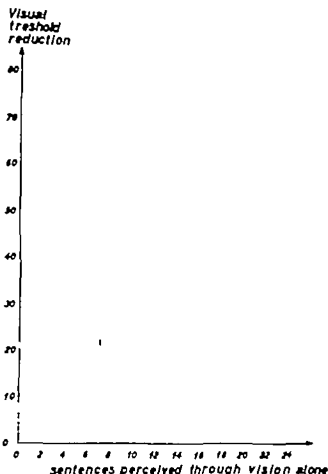


Fig. 2. The abscissa indicates how many sentences the patient is able to perceive through lipreading with out sound The ordinate shows by how many decibels the speech-reception threshold is reduced when the patient combines lipreading and hearing.

quence are presented on the TV screen without sound.

3 *Hearing and Vision Combined*

The 25 sentences are said by the speaker on the TV screen, and the sound is gradually increased in 10-dB steps from 20 dB below threshold to 20 dB above threshold.

The procedure of testing a patient is illus trated in Fig 1

CLINICAL MATERIAL

This preliminary report is concerned with the results in our first 100 patients representing all kinds of hearing disorders and with a speech-reception threshold varying from 30 to 70 dB the average being 50 dB (H. L.)

The relationship between vision and hearing was plotted in a diagram (see Fig. 2) Eighteen patients were so clever at lipreading that they were excluded from the diagram, because this group was not suitable in an investigation of the relationship between vision and hearing.

Fourteen patients did not understand a single sentence through lipreading alone, but nevertheless it is seen on the ordinate that the combination of hearing and vision improved their speech perception.

This is in good agreement with the fact that normally hearing persons also feel that they understand better when they are able to observe the face of the speaker

Fifty three patients are grouped in the lower part of the diagram. We found that the better the patients were at lipreading, the more could the intensity of the speech be reduced, still giving the patients 100 % perception.

The 15 patients represented by circles in the upper part of the diagram are a statistical mystery to us. We cannot explain why this group of moderately good lipreaders were able to communicate with the introduction of sound which was so faint that they merely perceived the rhythm of the message This suggests a certain capacity of combining the two senses of hearing and vision

The largest group consisting of 53 patients showed a fairly good correlation between lipreading ability and reduction of speech inten sity and perhaps we shall be able to express lipreading ability in physical terms of dB in the future, and with this aim in view we con tinue our work with the video-recorder

DISCUSSION

N Riskær Do you have any experience as regards the visual test with normal-hearing per sons?

Do you know how much training in lipread ing can improve the result in patients with impaired hearing?

H V Ewertsen (Reply to Riskær) Twenty five normally hearing subjects were examined in the preliminary research and a few of them were fantastically proficient in lipread ing.

Acta Otolaryng. 263 231 1970

CLICK EVOKED RESPONSES IN THE MEDIAL GENICULATE BODY IN AWAKE CATS

B. Ekholm, L. Olsen and K. Skrede

From the Institute of Neurophysiology, University of Oslo, Norway

A method for recording from the medial geniculate body in awake cats is reported. The pattern of the response was similar to that seen in anaesthetized cats. By using double clicks, there was depression of excitability following an excitatory response which lasted only 20–30 msec. Giving the animal barbiturate anaesthesia (30 mg/kg), the inhibitory period was greatly prolonged.

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EARLY DIAGNOSIS OF VIIITH NERVE TUMOURS BY ACOUSTIC REFLEX TESTS

H Anderson, B Barr and E Wedenberg

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Acoustic reflex tests were performed in 12 cases of tumour of the acoustic nerve and five tumours of the posterior fossa so located as to affect the nerve. The acoustic reflex threshold was pathologically elevated in all 17 cases, and in seven cases so much that the reflex could not be acoustically elicited. In the 10 cases in which the reflex threshold could be attained, the response showed an abnormally rapid fatigue on prolonged stimulation a phenomenon here termed "reflex decay" The observations indicate that the reflex-decay phenomenon is the earliest audiological sign of an incipient lesion to the acoustic nerve and hence it is of great value in the early diagnosis of acoustic tumours.

In clinical diagnosis, retrocochlear lesions in the form of acoustic tumours occupy a unique position. Interest in them is by no means related to their incidence on the contrary their proportion in a normal clinical audiological series is less than should be assumed from the abundant literature on the subject. At the Neurosurgical Clinic, Karolinska Sjukhuset, about 20 acoustic tumours are operated on each year More than half of the patients have such severe hearing impairment when referred for examination that a differential-diagnostic hearing test of any kind is out of the question. In relation to the total number of patients examined annually at the Department of Audiology of this hospital the chance of encountering a case with such audiometrically identifiable damage has a probability of less than 1 1000 This low incidence in itself implies a risk that these cases will be overlooked. Moreover recent investigations have shown that these tumours are not associated with such uniform audiometric patterns as was earlier believed particularly at the early stages (Johnson, 1966 Shapiro & Naunton, 1967)

Good agreement is normally regarded to be present between the subjective, "true" test of recruitment (e. g. Fowler's test) and the objective recruitment determination provided by the acoustic intra-aural reflex (Kristensen & Jepsen, 1952 Metz, 1952 Thomsen, 1955 Anderson & Barr 1966) Since the lack of recruitment is one of the salient features of retrocochlear hearing impairment (Dix *et al.* 1948 Goodman, 1957 Johnson & Sheehy 1966), it was considered of interest systematically to study the potentialities of this test for establishing an early diagnosis of disorders in the acoustic nerve.

MATERIAL

The series studied consisted of 17 patients with verified retrocochlear involvement with a hearing loss not exceeding 60 dB (mean 500 1000 and 2000 cps) Six of the patients still had a hearing threshold within the normal variation, when due regard was paid to age, sex and occupation In 12 cases the diagnosis was a tumour of the acoustic nerve five were classified as tumour of the posterior fossa with such a localization that they involved the acoustic nerve Of the cases, 15 were verified surgically and the remaining two were identified radiologically

METHODS

The equipment used for reflex measurement

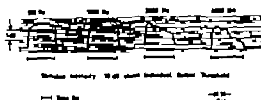


Fig. 1. The reflex response on prolonged stimulation recorded in a normal ear

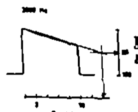
has previously been described by Klockhoff (1961) and Anderson (1969). Reference should be made to these papers for a more detailed account.

The acoustic reflex measurement can be used to solve a number of problems in hearing diagnosis of interest in the present context are the responses that can be recorded when the inner of the two intra-aural muscles, the *stapedius* muscle, is induced to contract. This muscle is the effecting organ in a reflex arc whose afferent pathway consists of the sensory cells of the cochlea and the acoustic nerve. In sound stimulation of moderate intensity a reflex contraction is elicited in the stapedius muscle, and the degree of concentration increases with the intensity of the stimulus within a fairly large dynamic range. The reflex response can thus be used as a measure of the afferent inflow through the sensorineural system of the ear at supra-threshold levels.

By ascertaining the lowest intensity at which recordable responses are obtained at different test frequencies—just as in the usual hearing threshold audiogram—a reflex-threshold curve is recorded. If then the stimulus tone is presented at definite levels above this reflex threshold, a relative measure of the strength of the muscle contraction in the form of response amplitude is obtained. These functions have been examined in previous studies, in which certain pathological criteria were also formulated.

Another interesting feature of the reflex response is its persistence on prolonged acoustic stimulation. Fig. 1 shows a representative recording in a normal ear: the test was performed at 500, 1000, 2000 and 4000 cps at a level of 10 dB above the reflex threshold and with a stimulus duration of 10 seconds. At the lower test frequencies no fatigue at all is observed in this period, at 2000 cps a small but significant reduction in the response amplitude is noted, and at 4000 cps this reduction is marked. This phenomenon has been termed "reflex decay". It is quantified as the time (in seconds) for the





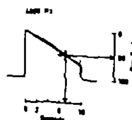


Fig. 2. Half-life points of responses indicated by continuous arrows: dash-dotted arrow is the limit of recording accuracy. Shaded area: Semi-interquartile range.

Table 1 *Result of differential-diagnostic hearing tests (acoustic tumours 12 posterior fossa tumours 5)*

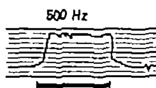
	Speech discr	Fowler's test	Threshold decay
Tested	17	14	16
Positive	8	9	8
Proportion of positive tests, %	47	64	50

response amplitude to be reduced by 50 per cent.

Fig 2 shows the mean persistence of the response for 50 ears of young subjects with normal hearing No reduction in response amplitude is observed for the lower test frequencies, whereas the median half lives of the responses for 2000 and 4000 cps are 14 and 7 seconds respectively (Anderson *et al* 1969)

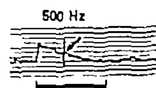
CASE H S

Left ear:





Right ear:





Tone On   1 Sec

Fig. 3 Recording of reflex decay in one of the acoustic tumour cases. In the left, normal ear no reflex decay is observed, and the response has here the characteristic rectangular configuration In the affected right ear the reflex decay is clearly seen, the half-life of response (indicated by arrows) is of the order of 4 seconds.

RESULTS

The results of the traditional hearing tests used in differential diagnosis namely speech discrimination, Fowler's test and the hearing threshold decay test, are found in Table 1 These tests were positive in only about 50 per cent of the applications, a degree of unreliability that is a well-documented feature.

As regards the results of the reflex measurements the reflex threshold was pathologically elevated in all 17 cases in seven cases so much that the reflex could not be elicited even at maximum available sound stimulus (120 dB hearing level)

In the 10 cases *in which the reflex threshold* could be attained however there was yet *another interesting feature in the reflex response* viz an abnormally rapid fatigue on prolonged stimulation As has previously been shown there is normally no measurable reflex decay for the frequencies *500 and 1000 cps.* For the tumour group there was a marked reflex decay the response amplitude *for these* frequencies being halved in about 3 seconds in none of the subjects at any of the test frequencies was the half life of response longer than 5 seconds (Fig. 3)

DISCUSSION

From the standpoint of reflex measurement there are thus two properties that are distinctive of the tumour group viz. an elevated reflex threshold and the described abnormally rapid decay in the reflex response

As regards unilateral elevation of the reflex threshold, this sign is not exclusively pathognomonic of retrocochlear lesions of this particular type Although very rarely encountered, *such elevation may be observed* for example in certain forms of sudden deafness" It is *thus evident that even though a unilateral pathological elevation* of the reflex threshold is *not entirely specific for expansive lesions* involving the acoustic nerve it should always *arouse suspicion of the presence of such a* lesion

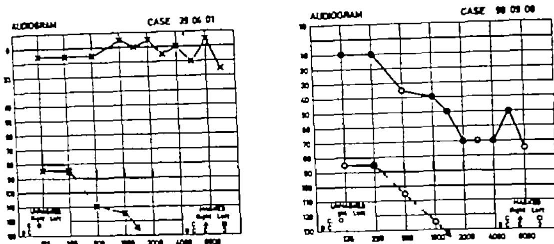


Fig. 4 Audiograms in two cases of retrocochlear lesio showing how reflex-threshold elevation may appear independently of hearing-threshold elevation.
Left audiogram: Woman, 23 years, with surgically confirmed tumour of the left posterior fossa.
Right audiogram: Man, 67 years, with surgically confirmed acoustic tumour on the right side.
Continuous curve is hearing threshold, reflex threshold dash-dotted with normal range shaded. I both cases, hearing and reflex threshold were within normal limits in the opposite ear

In this context, it is also important to discuss the seven cases in which no reflex response was obtained despite maximal acoustic stimulation. It was established in every case that the lack of reflex responses not merely depended on a conductive defect in the recording ear which prevented recording. As reflex responses of normal characteristics could be obtained by tactile or electrical stimulation, the possibility of a conductive defect in the recording ear could be ruled out.

In the cases in which the reflex threshold could be reached, the reflex threshold curves were fairly similar sloping from 125 cps and generally exceeding the working range of the audiometer at 1000 or 1500 cps. Even if no direct parallelism was present between the degree of hearing-threshold loss and elevation of the reflex threshold (Fig. 4) the tendency was nevertheless distinct. Thus, of the 10 cases in which the reflex threshold could still be reached, no less than six were found in the group with a hearing threshold of 20 dB or better

During the years that this study has been going on, the reflex-decay test has been performed in more than 600 patients in whom the clinical picture pointed to the possibility of a retrocochlear lesion, i. e., the greater part of the patients referred to our department for thorough otoneurological examination. In this biased case material of sensory defects in which a disproportionate number of retrocochlear lesions would be expected, only six additional cases of definitely pathological reflex decay were found. In none of these, however did the further medical examination disclose any signs of an expansive lesion. In these six cases, the traditional differential-diagnostic hearing tests were indicative of retrocochlear hearing impairment in two thirds of the applications, i. e a slightly higher proportion than in the group of verified tumours. There can be hardly any doubt that these patients also suffered from some form of impairment of the acoustic nerve although it was of a less specific nature.

A natural question in this connection is whether the cause of this fatigue is to be sought in the motor or sensory part of the reflex arc. The very fact that the reflex decay is dependent on the stimulus frequency suggests that the fatigue lies on the afferent side. Moreover

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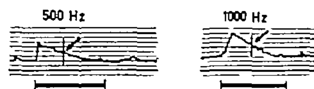
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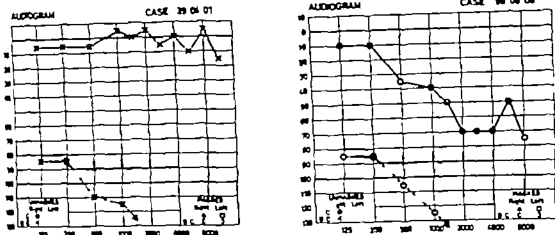


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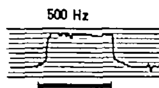
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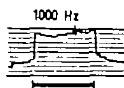
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thus is readily confirmed experimentally For even in the fatigue phase the full amplitude of the response is readily recovered by inserting complementary acoustic or tactile stimuli.

Naturally more moderate degress of reflex decay are occasionally encountered which, according to these primary criteria, cannot be classified as pathological in today's situation. Nevertheless, such cases merit considerable interest for future studies. This is especially true because recent research had confirmed that histologically demonstrable lesions of the acoustic nerve (including acoustic tumours) are far more common than can be inferred from their clinical manifestations, as revealed by the traditional audiometric tests (Moberg *et al.* 1969)

When using the reflex-decay test as a diagnostic tool, it must be borne in mind that the present investigations were made in cases of moderate hearing loss, i. e not exceeding 60 dB As regards extremely severe hearing impairment, cases of pathological reflex decay may occasionally be found in which it is not necessary or even reasonable to suspect the existence of an expansive lesion. This seems to be completely reasonable since such severe damage, even if it is primarily of hair-cell origin, would also be likely to lead to retrograde degenerative processes.

In contrast to the sensitivity of the reflex test in demonstrating a retrocochlear lesion we have the results of the customary psychoacoustic differential-diagnostic tests. Here we note a remarkably low score, despite the fact that the demands were very moderate for a result to be regarded as positive. Thus, for a positive outcome in the Fowler test, only an imbalance of 15 dB or more was required (at 500 1000 and 2000 cps or of these applicable test frequencies) In the threshold decay test, the corresponding requirement was a threshold shift of more than 25 dB (at 2000 cps or the nearest lower applicable test frequency) The speech-discrimination test was evaluated only on the basis of experience from the position and shape of the hearing threshold curve. Although the number of positive results of these three traditional tests increases with the degree of hearing-threshold impairment, the scatter is great and the deviations numerous.

From a general medical standpoint, the detection of retrocochlear disorder is obviously of the greatest importance. This is so because this hearing defect differs in a dramatic way from all other forms in that it indicates the possible existence of a lesion which, without surgical measures, is generally directly life-threatening. By means of the described relatively simple clinical test we are now able to screen out the very few possible tumour cases from the relatively large group of suspected cases. Moreover the reflex test has proved to be sensitive enough to identify these lesions at a very early stage. The importance of this possibility can scarcely be overestimated as early diagnosis is a prerequisite for a lenient surgical technique and a better prognosis (House, 1964 Fluur & Steiner 1969)

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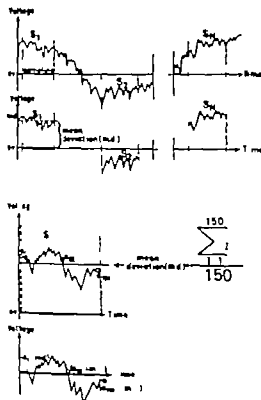


Fig. 1.

N, we accumulate the following values in the core memory

$$1)\ \sum_{n=1}^{N} a \qquad \sum_{n=1}^{N} a_{82,n} \qquad \sum_{n=1}^{N} a_{150}$$

$$2)\ \sum_{n=1}^{N} (a\ \ )^2 \qquad \sum_{n=1}^{N} (a_{82,}\ )^2 \qquad \sum_{n=1}^{N} (a_{150,n})^2$$

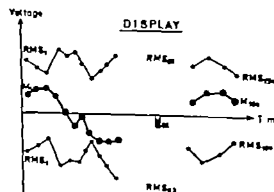
During the interval between stimuli we calculate the means, for instance Mean of the 82 eddresses, $M_{82,} = \frac{\sum_{j}^{n} a_{n,j}}{n}$ and these values are displayed on the oscilloscope screen on line.

EVALUATION OF EEG AMPLITUDE

The voltage measured in, for instance, the 82nd measuring point is different after each stimulus We have chosen the RMS values of this fluctuating voltage to represent the EEG amplitude of this measuring point, and the RMS value is calculated in every address using this formula (N indicating the total number of sweeps)

$$RMS_{82,n} = \sqrt{\frac{\sum_{n=1}^{n=N} (a_{82,n})^2}{N} - (M_{82,n})^2}$$

Fig. 2 shows the display obtained. The RMS value is purely numerical. The two mirrored curves on both sides of the X axis indicate the



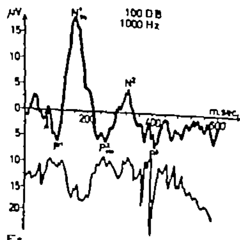


Fig.

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CLINICAL "ELECTRICAL RESPONSE AUDIOMETRY" ON A GENERAL-PURPOSE COMPUTER (IBM 1800)

G Salomon

From the Department of Otolaryngology and the Department for Data Processing in Medicine Copenhagen County Hospital Gentofte Denmark

A computer programme permitting the use of a general-purpose computer (IBM 1800) in evoked response audiometry has been developed. A DC coupling of the computer is obtained by digital parallel displacement of the sampling sweeps. EEG amplitudes (RMS) are calculated before and after stimulation. The V potentials in babies are facilitated by this DC coupling. In addition to the V potentials, a reduction in the EEG amplitude in response to sound indicates sound perception.

Evoked response audiometry (ERA) is often difficult in children. The V potential varies partly due to movement artifacts partly because the response has an uncharacteristic shape. The electronegative component N^1_{100} at a latency of 100 msec. and the P^2_{200} are often not prominent On the other hand, the late positive components with long duration are marked To facilitate the presentation of the slow positive components a DC recording system with time constants of 3–10 sec. would be desirable

In EEG audiometry any reproducible change in the EEG in response to sound stimulation indicates sound perception (Derbyshire 1964) Thus, our general-purpose computer programme (Skogstad Nielsen *et al* 1970) has been designed to calculate simultaneously both the usual summation and the amplitude of the EEG (RMS) during the sampling time

THE DC PROBLEM

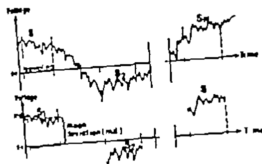
Our analogue to digital converter (ADC) will digitalize values between ±5 volts into ±32,000 digits.

We found that a DC-coupled EEG amplifier with a gain of 10 000 rarely exceeded these limits and mostly gave AC components of approx 250 mV As the EEG recording was performed with 1 % accuracy and as 250 mV on our ADC gave 400 digits, we normally divided our digital values by 4 In a few patients larger DC changes occurred. This was overcome by decreasing the EEG-amplifier gain by a factor 2 or 4 and dividing the digital values by a correspondingly smaller number

Fig. 1 shows schematically an EEG recorded with a time constant of 10 sec. S_1 S_2, S_N are sampling sweeps to be summated. Due to the DC recording these sampling sweeps have a mean deviation of (MD) volts from 0 volt. If 150 measuring points are used for digitalization of each sampled sweep, the mean deviation

(MD) is $\dfrac{\sum_{I=1}^{150} a_I}{150}$

If this deviation is subtracted from each measured value in the S_1 sweep a parallel displacement of the S_1 sweep is obtained. A similar parallel displacement is performed in all sweeps. During further calculations the values of a_1 a_2, a_{150} are replaced by the corrected values $(a_1 - MD)$ $(a_2$ $MD)$ $(a_{150} - MD)$ The value $(a_1 - MD)$ is indicated by $a_{1\,1}$ The member in the nth sweep is indicated by a_I If we still use 150 measuring points, and if we call the total number of stimuli



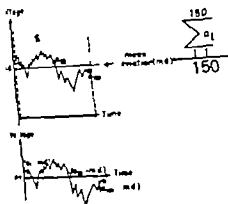


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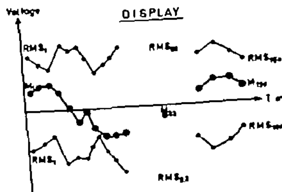
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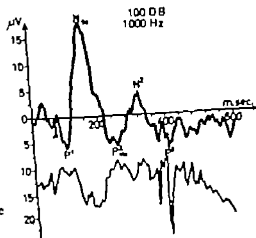


Fig 2.

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CLINICAL "ELECTRICAL RESPONSE AUDIOMETRY" ON A GENERAL PURPOSE COMPUTER (IBM 1800)

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A computer programme permitting the use of a general-purpose computer (IBM 1800) in evoked response audiometry has been developed. A DC coupling of the computer is obtained by digital parallel displacement of the sampling sweeps. EEG amplitudes (RMS) are calculated before and after stimulation. The V potentials in babies are facilitated by this DC coupling. In addition to the V potentials, a reduction in the EEG amplitude in response to sound indicates sound perception.

Evoked response audiometry (ERA) is often difficult in children. The V potential varies partly due to movement artifacts, partly because the response has an uncharacteristic shape. The electronegative component N^1_{100} at a latency of 100 msec. and the P^2_{200} are often not prominent. On the other hand, the late positive components with long duration are marked. To facilitate the presentation of the slow positive components a DC recording system with time constants of 3–10 sec. would be desirable

In EEG audiometry any reproducible change in the EEG in response to sound stimulation indicates sound perception (Derbyshire, 1964) Thus, our general purpose computer programme (Skogstad Nielsen *et al* 1970) has been designed to calculate simultaneously both the usual summation and the amplitude of the EEG (RMS) during the sampling time.

THE DC PROBLEM

Our analogue to digital converter (ADC) will digitalize values between ±5 volts into ±32 000 digits.

We found that a DC-coupled EEG amplifier with a gain of 10 000 rarely exceeded these limits and mostly gave AC components of approx. 250 mV As the EEG recording was performed with 1 % accuracy and as 250 mV on our ADC gave 400 digits, we normally divided our digital values by 4 In a few patients larger DC changes occurred This was overcome by decreasing the EEG-amplifier gain by a factor 2 or 4 and dividing the digital values by a correspondingly smaller number

Fig. 1 shows schematically an EEG recorded with a time constant of 10 sec S_1 S S_x are sampling sweeps to be summated Due to the DC recording these sampling sweeps have a mean deviation of (MD) volts from 0 volt. If 150 measuring points are used for digitalization of each sampled sweep the mean deviation

$$(MD) \text{ is } \frac{\sum_{I=1}^{150} a_I}{150}$$

If this deviation is subtracted from each measured value in the S_1 sweep a parallel displacement of the S_1 sweep is obtained. A similar parallel displacement is performed in all sweeps. During further calculations the values of a_1 a a_{150} are replaced by the corrected values $(a_1 - MD)$ $(a_2 - MD)$ $(a_{150} - MD)$ The value $(a_I - MD)$ is indicated by $a_{I\,1}$ The member in the nth sweep is indicated by a_I If we still use 150 measuring points, and if we call the total number of stimuli

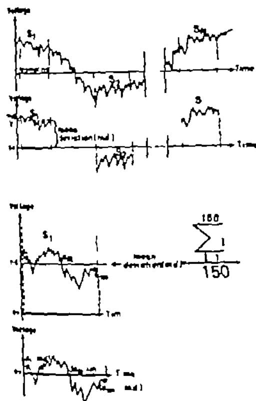


Fig. 1.

N, we accumulate the following values in the core memory

1) $\sum_{n=1}^{N} a_{1,n}$ $\sum_{n=1}^{N} a_{82,n}$ $\sum_{n=1}^{N} a_{150,n}$

2) $\sum_{n=1}^{N} (a_{1,n})^2$ $\sum_{n=1}^{N} (a_{82,n})^2$ $\sum_{n=1}^{N} (a_{150,n})^2$

During the interval between stimuli we calculate the means, for instance Mean of the 82 addresses, $M_{82} = \dfrac{\sum_{j=1}^{j=n} a_{82,j}}{n}$ and these values are displayed on the oscilloscope screen on line.

EVALUATION OF EEG AMPLITUDE

The voltage measured in, for instance, the 82nd measuring point is different after each stimulus. We have chosen the RMS values of this fluctuating voltage to represent the EEG amplitude of this measuring point, and the RMS value is calculated in every address using this formula (N indicating the total number of sweeps)

$$RMS_{82,x} = \sqrt{\frac{\sum_{n=1}^{n=N} (a_{82,n})^2}{N} - (M_{82,x})^2}$$

Fig. 2 shows the display obtained. The RMS value is purely numerical. The two mirrored curves on both sides of the X axis indicate the

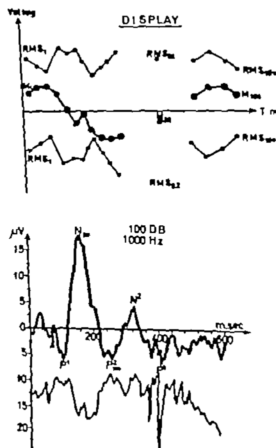


Fig. 2.

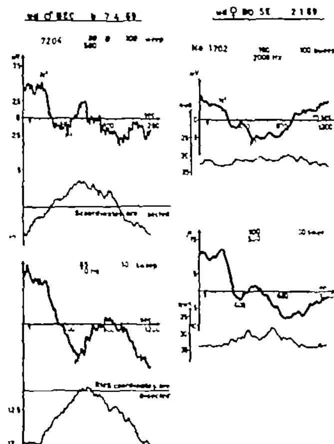


Fig. 3 Summated curves (fat line) and RMS curves in response to sound stimuli (arrow). Left, from a - week-old baby right, from a 3-month-old baby

Fig 3 shows curves obtained from two different children. The summated curves to the left from a baby only a few weeks old show at about 140 msec. a sudden change from negative to positive values. (N¹?) followed by a nearly square-wave-shaped curve. We have often seen a small positive peak in the middle of the square wave. A very similar response pattern is shown to the right. It is from a 3-month-old baby The baby to the left showed a very marked type 2 pattern of the RMS curve.

RMS values While the upper part of the figure is drawn schematically the lower curves are obtained from a normal adult person.

RESULTS

The lower part of Fig. 2 shows a V potential (fat curve) in response to a sound stimulus (arrow) and one of the curves through the RMS values. We have found two types of changes in the RMS value in response to sound stimulus.

Type 1 occurs when the components of the V potential are large, as compared with the running EEG thus augmenting the RMS value of the EEG Note the bump opposite N^1_{90}

Type 2 representation of sound perception is present when a decrease in EEG amplitude is demonstrated on the RMS curve.

After sound application (arrow) the curve is arch-shaped showing a transient decrease in EEG amplitude.

Twenty severely deaf psychiatric male and female patients in whom conventional audiometry was uncertain were tested with ERA. The average age was 34 years. Only one patient had clinical anacusis, and ERA showed no response In 13 patients, the average difference in the threshold of 500 1000 and 2000 cps

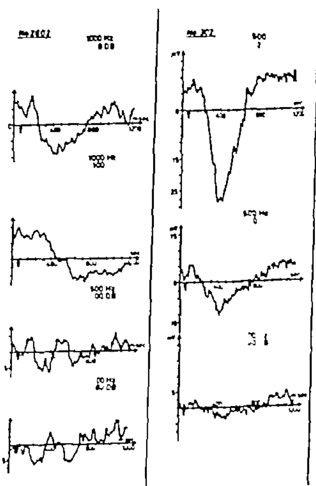


Fig. 4 Summated curves in response to sound stimuli (arrow) from two different patients with severe mental disorders.

was 6 dB or less. In four patients, the ERA was 20–30 dB better than conventional, in one 15 dB and in another 30 dB poorer. Thus, we found either a very good correlation or a marked difference between ERA and conventional audiograms. In the V potentials from the patients with severe mental disorders we often found a marked resemblance of the infantile V potentials.

The left and right sides of Fig. 4 show summated curves from two patients in this group. The N¹ is relatively small or absent, and a DC component is a prominent feature of the response.

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DISCUSSION

Krogh. We have stimulated neonates with a high intensity (80–100 dB sensation level) and the response showed P N peaks with a latency period of 400–500 msec. Can you, on the basis of your experience, say whether this might be an evoked response from a tactile stimulation?

G. Salomon (Reply to Krogh). I think the late positive component was elicited in response to sound, as only 50 dB on free field was active in small children.

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REGISTRATION OF ACOUSTICALLY EVOKED VERTEX POTENTIALS WITH UNCONVENTIONAL AVERAGING TECHNIQUE

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The recording of acoustically evoked EEG potentials is normally considered to be dependent on an electronic average computer The present paper describes a measuring set up for such registrations without use of a conventional averaging technique. The repetitive signals are displayed on an oscilloscope with a camera attachment supplied with a special lens system The image obtained by superposition of the individually displayed traces will under appropriate conditions disclose the true average of the received evoked potentials. Some examples are given to illustrate the clinical applicability of the method.

The applicability of recordings of the vertex potential in hearing tests relies on repetitive *measurements The faint voltage variations* produced by weak acoustic stimuli are concealed by the spontaneous activity known as the EEG The customary procedure to disclose the acoustically evoked potentials involves an electronic computer to calculate the average response to a series of identical stimuli

A simple presentation of several signals may be recorded as superimposed traces on an ordinary oscilloscope with a camera attachment. These superimposed traces, although occasionally disclosing the response do not abolish the need for an average recording It is, however possible to modify the photographic procedure so that the bundle of individual traces is replaced by a continouous band which may be chosen to reveal the arithmetic mean or the median as desired

The principle is based on a controlled dispersion of the image forming light in the direction of the y-axis. To *obtain the arithmetic* average a cylinder lens with a suitable rhombic aperture (fig 1) may be used instead of the ordinary photographic objective. A curve displayed on the oscilloscope will hence produce an image shaped as a band with an illumination falling off linearly towards the edges. The light distribution along a horizontal line through this band will be seen to exhibit intensity variations exactly corresponding to the signal pattern *When more sweeps follow* these light distributions will add up and on the photographic film expose the sum of the successive signals along the horizontal line. Owing to the linear slope of the light intensity the true aver*age of all the sweeps will also appear as a* curve following an appropriate constant exposure value on the film

One of the procedures that will produce the necessary light distribution is outlined in Fig. *1 The cylinder lens combined with the rhombic* aperture will thus constitute the necessary in

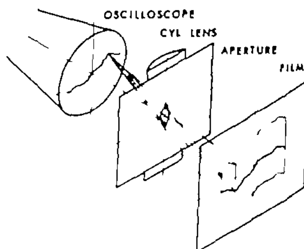


Fig. 1 Diagram of a system for optical formation of arithmetic mean of traces displayed on an oscilloscope

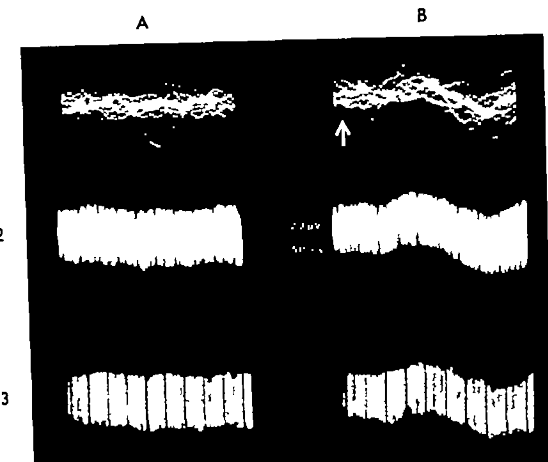


Fig. 2. Example of a recording from a normal person. 1. 20 superimposed traces, 2, band representing arithmetic mean of these traces; 3. band representing the median of the same traces. A, without stimulus; B, with stimulus 1000 Hz, 10 dB above subjectively determined threshold.

struments for the formation of the arithmetic mean. It is, however, only necessary to replace the shown aperture with a rectangular one if it is wanted to obtain the median value instead of the arithmetic mean. The well-known advantage of the median as compared to the arithmetic mean in physiological measurements is the insensitivity to noise peaks. This noise eliminating feature will be further supplemented in any of the described optical procedures because excessively large noise peaks will simply offset the tracing out of the average-forming band.

Our present technique allows the simultaneous recording of (1) all the individual traces, (2) the arithmetic mean, and (3) the median.

Next to these recordings, on the same polaroid picture, is a control series (no stimulus) as seen in Fig. 2.

This is the basis of the new optical data processing, but significant extensions including multichannel recording, frequency analysis, pattern recognition and correlation analysis are in development. It should be mentioned that the described average-forming technique may be applied at considerably less costs than currently available electronic computers.

The successful application of the ERA depends on reliable electrode connections to the patient. The necessary low electrode resistance (1000–6000 ohms between two electrodes measured at approx. 100 mV 500 Hz) appears to be conveniently obtained with skin electrodes of german silver 18 mm dia., and an electrode

Table 1 *31 ears (16 persons)*

Intensity	< 20 dB	20–30 dB	> 30 dB
Pos. responses	24	3	4

jelly composed of Elema Mingograph Cream plus a few per cent Bio-Tex (an ordinary enzyme based washing powder)

In order to test the described apparatus for objective assessment of hearing we have examined 40 patients aged from 6 to 37 years.

The method of the examination is as follows The patients are examined awake lying on a couch in a sound-proof room They are asked to count the number of sound stimuli used After washing of the skin the electrodes are fixed by means of the above mentioned electrode paste and tape.

During the first period vertex frontal recording was used The placing of the electrodes is now in accordance with the standard the potentials being recorded between the vertex and the left mastoid

The resistance between the electrodes is measured in each investigation We have in all cases, if necessary repositioning the electrodes achieved a resistance below 6000 ohms, and in 12 cases we have found values below 2000 ohms. In order to obtain a significant response it is of great importance to achieve the lowest possible resistance.

Previous to the examination the hearing level of the patient is determined in the conventional manner

The stimulus used is a pure tone of 1000 Hz with approx. 25 msec. onset and of 500 msec. duration The tone is applied at 10-second interval and is repeated 20 times. The patient is stimulated monaurally and the traces on the oscilloscope are photographed. On the same picture 20 sweeps without stimulating the patients are recorded as a control

Our series consists of 40 persons, aged from 6 to 37 years, with normal hearing in whom 78 ears were examined. In the first group of the series, potentials were recorded between the vertex and the frontal region In the second group recording was made between the vertex and the mastoid In group 1 (16 persons 31 ears) significant evoked responses were obtained in 24 cases after stimulation up to 20 dB above the hearing level Intensities between 20–30 dB produced response in three cases. No significant evoked response was obtained in four cases, but it must be added that in these cases stimuli exceeding 30 dB were not used (Table 1)

Group 2 comprised 24 persons (47 ears) Only stimuli of 10 dB above the thresholds were used in this group Table 2 shows that in no less than 43 out of 47 ears a positive response was elicited, and that no response was obtained in four cases (Table 2)

The clinical importance of this method can be illustrated by the following case of psychogenic deafness

A 21 year old soldier complained after shooting of total deafness in the left ear He had been examined several times with reference to his loss of hearing, which was interpreted as real. With a view to the claim for compensation the patient was again referred to examination Pure-tone audiometry showed continuously no hearing in the left ear Evoked-response audiometry produced significant responses from both ears when stimuli of 15 dB above normal hearing level was used. The examination was carried out only at 1000 Hz. The stapedius reflexes of the patient were examined and found normal in both ears with homo- as well as contralateral stimulation Hence this examination confirms the hearing threshold of the patient as obtained by means of the EEG audiometry

This method of optical average recording in electrical response audiometry has been used only for a short period, and only a few patients have been examined Though based on a limited experience it is indicated that instrumentation of this type will prove valuable in future clinical investigations.

Table 2 *47 ears (24 persons)*

Responses after stimulation 10 dB above hearing threshold	Positive	Negative
Number of ears	43	4

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EVOKED RESPONSES TO SISI STIMULI

CONTRALATERAL MASKING EFFECTS

P Osterhammel, K. Terkildsen and P Arndal

From the Department of Otolaryngology the U iversity Hospital, Copenhagen Denmark

Evoked cortical responses to Sisi-type stimuli at 20-dB sensation level and increment magnitudes 2, 3 and 5 dB tend to be enhanced by the application of contralateral masking noise. With 5 dB increments and the continuous tone at the threshold of hearing the same masking noise caused the response to disappear The enhancement of auditory discrimination at suprathreshold levels through application of contralateral masking and the central masking effect" at the threshold are thought to be comparable to the so-called indirect adaptation mechanism of the ey and an indication that the efferent innervation to the cochlea is important for the adaptation of the ear

In the field of sensory physiology the phenomenon of adaptation was first demonstrated for the sense of vision. It was shown that as an integral part of this process adaptation to strong light would at the same time cause a reduced sensitivity to faint light and an elevation of the threshold for light perception.

Investigations on the sense of hearing has pri marily been concerned with this negative side of adaptation in the form of changing loud ness function and the widely used tone-decay tests.

The positive aspects of adaptation become apparent when contrast thresholds are deter mined. An adapted eye possesses a better discrimination and more just noticeable differ ences (JNDs) within the dynamic range to which it is adapted.

The so-called direct adaptation is caused by light which strikes those parts of the retina that are tested. This is different from indirect adaptation, where the performance in the test area is influenced by light that illuminates other parts of the retina, and thus involves neural mechanisms.

In audiology the Jerger SISI test represents an analogy to direct adaptation. The ear is exposed to a constant tone, and the ability to differentiate is measured by the number of increments which the patient can detect. It is a measurement for difference limen of intesity (DLI) in the adapted state.

Blegvad and Terkildsen (1967) showed that contralateral masking would improve the DLI in the middle and high-frequency range, when it was measured by this method. Here we apparently have an analogy to the indirect adaptation of the eye. In order to attain a sufficient degree of accuracy in these investigations the statistical threshold function was deter mined by means of psychometric curves.

The detection of evoked slow cortical potentials as a response to sensory stimuli has opened up interesting possibilities of objective comparisons of the very magnitude of sensory perceptions, instead of being limited to deter minations of the threshold. In the present investigation, we measured the cortical response to tone increments and how this response would be influenced by contralateral masking.

The equipment for measuring the slow evoked potentials was based on a Mnemotron CAT computer with 400 channels. The EEG electrodes were made of German silver with a 6 cm² electrode area. Electrode placement vertex/mastoid process and ground to the other mastoid process. Amplification 100 000 times

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by two amplifiers in series The pre-amplifier was of the differential type with an input impedance of 100 M-ohms and a high common mode rejection in order to ensure an optimal cancelling of in phase signals The main amplifier was supplied with various selective filters, amongst others for the line frequency Frequency range 0 1–30 cps.

The test programme made it necessary to record the whole procedure by means of a DC tape recorder at the same time as the on-line computer averaging For the write-out we used a X Y plotter In order to permit exact measurements, the set-up was supplied with a calibration unit controlled by the X sweep of the computer and on each curve a summated calibration pulse was automatically recorded at the end of the "window" The tones came from a Madsen OB 60 audiometer and the increments were controlled by a photo-electric device (Blegvad 1966) To this was added an extra trigger unit to start the computer and supply the DC recording with pulses necessary for the off line analysis

The cortical response to strong stimuli is well defined especially with regard to latency When the stimulus gets close to threshold the response becomes much more variable which is obviously particularly detrimental for work with an averaging technique In order to reduce this variability we tried to keep the test conditions as constant as possible The investigation was conducted in a darkened sound proof room The subject rested in a reclining comfortable chair with support of the neck and the feet

Evoked responses were recorded for increments of 2, 3 and 5 dB at 20 dB SL and with the frequencies 1000 and 4000 cps. The increments had a duration of 200 msec and rise fall times of 50 msec, as in Jerger's test. In order to shorten the procedure the intervals were only 2.5 sec The increments were presented in series of 50 and there were a total of 10 such series for each increment magnitude at both frequencies During every other series, the contralateral ear was exposed to 80 dB

Table 1

	1000 cps			4000 cps		
Increments, dB	2	3	5	2	3	5
Subject A			++			
Subject B	+		−			
Subject C		+			++	

masking noise Thus, each measurement is based on a comparison between five series with and five series without contralateral noise After each series there was an intermission of 2 minutes, during which the averaged response from the computer was recorded

In order to maintain a steady level of attention the subjects were requested to count the increments.

As already mentioned the procedure was taped by means of a DC recorder This permitted a separate averaging of all 250 responses with and without contralateral noise.

A programme with 10 series permits a statistical evaluation of the results from each session separately by the Student method We decided to use a single parameter which included both the response magnitude and the latency The response magnitude was measured as the difference between N_1 and P_2 in microvolts and divided by the latency to P_2 in msec. As N_1 we would accept the largest negativity in the time area 100 to 230 msec and as P_2 the largest positivity between 180 and 400 msec after stimulus onset

The results are seen in Table 1 in which + and ++ indicate that the evoked response was larger with contralateral noise and at statistical confidence levels of 5 % and 1 % respectively − indicates that, under similar circumstances, the response was smaller at the 5 % level

It should be mentioned that the evoked response to such weak stimuli is relatively small and the signal to noise ratio often unsatisfactory The results can therefore only be taken as an indication of what actually takes place by the application of contralateral noise A

more complete description of the function would necessitate much larger series.

The results from counting the increments is only of interest for the 2 dB stimuli, which were at the threshold of audibility In all instances, the subjects would detect more increments when contralateral noise was present, and there was good agreement between the subjective and objective findings.

It is well known that contralateral noise causes an elevation of the threshold for hearing. This so-called central masking effect was demonstrated objectively in the following way The constant tone was set at the hearing threshold and the increments at 5 dB In two of the subjects, these increments evoked a clear cut response, which, however disappeared as soon as contralateral noise was introduced. Also this objective finding corresponded to the subjective listening results.

If we return to the introductory remarks about adaptation of the eye, our findings with regard to the effect of contralateral masking noise appears to be very similar to the so-called indirect adaptation, and this applies both to the improved DLI above threshold as well as the elevation of the threshold itself.

Ever since the anatomical detection of the dense efferent innervation to the organ of Corti, there have been speculations about the psychophysical correlate, or in other words, the meaning of this arrangement. Our findings show that the adaptation level in one ear is partly determined by the other and it seems natural to see this as one function of the efferent innervation.

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EEG-COMPUTER AUDIOMETRY (ERA) IN A GROUP OF PRE-SCHOOL AND SCHOOL AGE CHILDREN

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A study of average evoked responses in a number of normal, mentally retarded and aphasic pre-school and school children is reported. The purpose was to evaluate this new technique in order to apply it as a possible objective audiometric method in general or in a limited group of children An averaged evoked response was recorded from the vertex electrode in all the children tested Comparisons were made be tween ERA and audiometric thresholds. Our experi ence leads us to place considerable confidence in electrophysiologically determined threshold measure ments.

The description below deals with a study in evoked response audiometry (ERA) The main purpose of this study was to examine the use fulness of the ERA method in general and to compare it with the ordinary audiometry We were particularly interested in this method for the use in children s audiometry

Our clinical group consisted of 65 pre school and school age children, viz. 42 boys and 23 girls Of these 44 were considered normal apart from their hearing impairment 13 were aphasic of the impressive or expressive type and 8 were mentally retarded.

The ages of the children ranged from 2 to 16 years and averaged 8 3 years. Standard audiograms were available for 44 of the chil dren, and the time which had elapsed from the evaluation of the standard audiogram averaged approx. 4 months.

Electrode Placement

The ongoing EEG activity was picked up by scalp solder-disc electrodes attached to the head with EEG electrode paste and pulverized pumicestone In small and restless children the electrodes were held in position with col lodium The signal electrode was placed in the vertex with the mastoid process as reference and the ground electrode was placed fron tally

Before the start of the test the electrode resistance was approx 1000 ohms, which later increased slightly

Test Procedure

The measurements were made in a normal audiometry room the patient was sitting in a comfortable armchair in a reclined position (Fig. 1) Small children were preferably sitting on the mother's lap or they were playing with toys on the floor Most of the children were remarkably co-operative and quiet throughout the examination. The duration of the test was $1^1/_2$–2 hours.

Stimuli

The stimuli consisted of non-click tone pulses with frequencies of 500 1000 and 4000 cps The total length of the tone pulse was 400 msec with a rise and decay time of 25 msec. each Normally the stimuli were delivered at a rate of one every 3 sec. and each stimulus was presented 100 times. The EEG was moni tored on an oscilloscope in order to test the general condition of the patient and the elec trodes, after which the evoked signal was fed into the computer (T M I CAT 400 C) and

the first 500 msec. of the response was analysed and then the sum response plotted out on a level recorder (Figs. 2 and 3).

Running

The procedure for establishing the threshold response varied somewhat as the examiner gained experience in the technique. At first we started with a stimulus of high sound intensity to make sure of obtaining a well-defined responses, which were significant at the thresh-stimulus to the ERA threshold, but during the latter part of the test we discovered some false results, as well as rather poorly defined responses, which were significant at the threshold level, probably due to habitation, fatigue of the patient, and/or drying of the electrode paste. The latter problem was solved by keeping the electrodes moist with the aid of small pieces of rubber sponge. The former was solved by using a somewhat different stimulation procedure. Firstly by giving a high and then a low intensity level. A high intensity of about 80 dB sensation level to give a clear response as a guide to the threshold response. The low intensity must be determined by the experienced examiner. If there is no response from this low intensity then the average of the

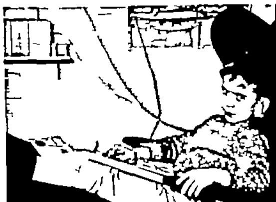


Fig. 1. ERA test in seven year old boy sitting in a comfortable armchair playing with toys.

two values should be tried. Should, however the response be positive, then the attenuator should be decreased in 10 dB steps.

In cases where we experienced difficulty in determining the threshold, we found it advantageous to increase the number of stimulations by for instance, 50. This also resulted in minimizing the influence of a high background activity.

The presence or absence of the response was judged "on-line" from the response pattern on the computer display and the new intensity and frequency were selected according to this.

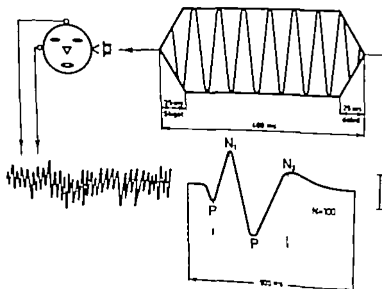


Fig. 2. The tone pulse is delivered to the patient's ear. Below left, the evoked response with the noisy background activity; right, the averaged evoked response after 100 shots.

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EEG-COMPUTER AUDIOMETRY (ERA) IN A GROUP OF PRE SCHOOL AND SCHOOL AGE CHILDREN

H Economopoulou, H J Krogh and L. Fosvig

From the Research Laboratory for Technical Audiology of the State Hearing Centres Odense County and City Hospital Odense Denmark

A study of average evoked responses in a number of normal mentally retarded and aphasic pre school and school children is reported. The purpose was to evaluate this new technique in order to apply it as a possible objective audiometric method in general or in a limited group of children An averaged evoked response was recorded from the vertex electrode in all the children tested. Comparisons were made between ERA and audiometric thresholds. Our experience leads us to place considerable confidence in electrophysiologically determined threshold measurements.

The description below deals with a study in evoked response audiometry (ERA) The main purpose of this study was to examine the usefulness of the ERA method in general and to compare it with the ordinary audiometry We were particularly interested in this method for the use in children s audiometry

Our clinical group consisted of 65 pre-school and school-age children, viz. 42 boys and 23 girls. Of these, 44 were considered normal apart from their hearing impairment 13 were aphasic of the impressive or expressive type and 8 were mentally retarded.

The ages of the children ranged from 2 to 16 years and averaged 8 3 years. Standard audiograms were available for 44 of the children, and the time which had elapsed from the evaluation of the standard audiogram averaged approx 4 months.

Electrode Placement

The ongoing EEG activity was picked up by scalp solder-disc electrodes attached to the head with EEG electrode paste and pulverized pumicestone In small and restless children, the electrodes were held in position with collodium The signal electrode was placed in the vertex with the mastoid process as reference and the ground electrode was placed frontally

Before the start of the test, the electrode resistance was approx 1000 ohms, which later increased slightly

Test Procedure

The measurements were made in a normal audiometry room the patient was sitting in a comfortable armchair in a reclined position (Fig. 1) Small children were preferably sitting on the mother s lap or they were playing with toys on the floor Most of the children were remarkably co-operative and quiet throughout the examination. The duration of the test was 1 1/2–2 hours.

Stimuli

The stimuli consisted of non-click tone pulses with frequencies of 500 1000 and 4000 cps. The total length of the tone pulse was 400 msec with a rise and decay time of 25 msec. each Normally the stimuli were delivered at a rate of one every 3 sec. and each stimulus was presented 100 times. The EEG was monitored on an oscilloscope in order to test the general condition of the patient and the electrodes, after which the evoked signal was fed into the computer (T M I CAT 400 C) and

the first 500 msec. of the response was analysed and then the sum response plotted out on a level recorder (Figs. 2 and 3)

Recording

The procedure for establishing the threshold response varied somewhat as the examiner gained experience in the technique. At first we started with a stimulus of high sound intensity to make sure of obtaining a well-defined responses, which were significant at the thresh-stimulus to the ERA threshold, but during the latter part of the test we discovered some false results, as well as rather poorly defined re sponses, which were significant at the threshold level, probably due to habitation, fatigue of the patient, and/or drying of the elec trode paste. The latter problem was solved by keeping the electrodes moist with the aid of small pieces of rubber sponge The former was solved by using a somewhat different stimula tion procedure. Firstly by giving a high and then a low intensity level. A high intensity of about 80 dB sensation level to give a clear response as a guide to the threshold response The low intensity must be determined by the experienced examiner If there is no response from this low intensity then the average of the



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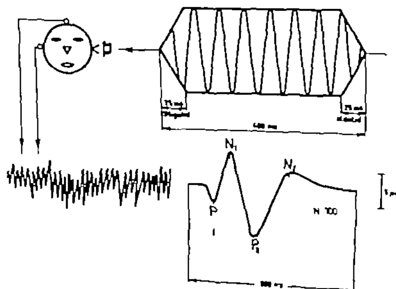


Fig. 2. The tone pulse is delivered to the patient's ear Below left, the evoked response with the noisy back ground activity right, the averaged evoked response after 100 shots.

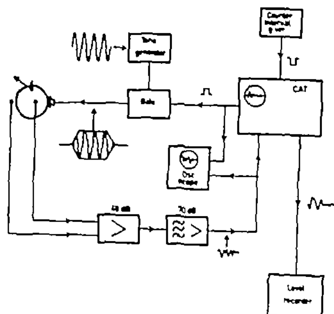


Fig. 3. Principle diagram of the apparatus used for the ERA test.

RESULTS

The recordings were mainly analysed for the purpose of deciding the ERA threshold. This was determined as follows. That pulse tone intensity which showed response whereas a pulse tone of 5 dB lower intensity did not. All the 65 children examined showed characteristic responses. This was defined as a three phasic wave form which started with a positive deflection or peak P_1 at about 100 msec. after the start of the stimulus, a negative, N_1 at about 150 msec. and another positive P_2 at about 250 msec.

By comparing the individual recordings we found small deviations from person to person, and sometimes also from the first to the last recorded response at the same intensity and in the same person.

Special attention was paid to the evaluation of the responses elicited in mentally retarded and aphasic children for the purpose of disclosing possible significant variations from normal, but there were no large differences in the three groups.

It was ascertained that a reduction in the stimulus intensity resulted in a decrease in the response amplitude and an increase of the latency time. The threshold response may occasionally be somewhat uncertain and in such cases it will be necessary to compare this with an evoked response of high intensity together with a display of the background activity. If this is fairly high, it may be necessary to increase the number of stimuli.

A few of the children were rather restless during the test, but nevertheless we obtained responses. In these particular cases, the major problem was to fasten the electrodes and to place the telephone. In some cases, we decided to use a free field signal. With reasonable probability, we obtained responses in 51 children at three frequencies, in 12 children at two frequencies, and in two children at one frequency. The absence of response was due to the threshold being beyond the measuring range of the audiometer or due to lack of time and to the presence of a high background activity.

Comparison between the ERA threshold and the standard audiometric threshold obtained for the same ear showed a mean difference of 2 dB (ERA minus normal values).

Conclusion

This preliminary investigation indicated that ERA will be a useful instrument for the examination of the human hearing in unco-operative cases. At the same time we have a remedy in the differential diagnosis between deafness and aphasia. However, it must be noted that the ERA method, on account of the relatively long examination time required, is only justified in special cases in which normal methods cannot be used with advantage.

Finally, we may remark that a tool has been placed into our hands which opens up the possibility of investigating part of the hearing mechanism even in neonates. This is of great significance especially for children in the risk group.

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EVOKED-RESPONSE AUDIOMETRY

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Within the last decade, evoked-response audiometry (ERA), based on recording of acoustically evoked cortical potentials, has become increasingly common in the audiological clinic. This technique, however must still be considered to be at the experimental stage, and it is at present difficult to foresee the advances which the use of this method will introduce into audiological work.

In this technique, it is important, before the test is undertaken, to take the following questions into account: What is the purpose of the test? What use is going to be made of its results? A test should not be performed simply for the sake of prestige. The more complicated an investigation is, the more important is the assessment of the expected results.

After an analysis of the scope and purpose, the method should be adjusted in accordance with the expected usefulness. From a technical point of view it must be considered irrational to carry out a series of complicated and time consuming investigations which exhaust both the patient and the examiner if there is not a reasonable possibility that the results of the test can provide data with a bearing on the therapy

ERA is complicated by the weakness of the evoked potentials, as compared with the general electrical activity of the brain and the muscles. We may regard this activity as a strong background noise which interferes with the measurements, and which it is necessary to suppress in order to determine the evoked potential. This is commonly done by the special computer technique of averaging the results of several repeated tests. The background noise can be considered random in nature and will by this method approach zero, whereas the evoked potential will increase. After for example, 100 repetitions, the signal-to-noise ratio will theoretically have improved by 20 dB

The presence of the background noise will introduce a factor of uncertainty in the determination of the evoked potential. For the acquisition of a greater accuracy in our knowledge of this potential a better signal-to-noise ratio and, hence a larger number of repetitions are required. It is not uncommon to use 50–100 repetitions, and as experience shows that the interval between the applications of stimuli must be at least 3 seconds, the ERA test requires a considerable period of time, which is one of the greatest disadvantages of the method.

It is most probable that a detailed knowledge of the evoked potential as a function of time will enable us to obtain information of importance in diagnosis, and that the determination of the response amplitude as a function of the stimulus intensity may reveal further information as to the normal and pathological functions of the sense of hearing. However the present experience in this field is limited, but a great amount of work and ingenuity is devoted to research into the problems involved.

At the present time, ERA is most commonly used in audiological work in order to reveal whether a patient responds to an acoustical

stimulus or not, thus making it possible to record audiograms in unco-operative subjects, such as children mentally retarded patients and malingerers. This reduced scope may result in several advantages, because it is unnecessary to obtain a detailed record of the evoked potential as a function of time the only necessity being a determination whether a response is present or not. This can be done with fewer repetitions, especially when the measurements are performed by a trained and experienced examiner

Furthermore it must be expected that an increase in the signal to-noise ratio can be accomplished by electrical filtering of the recorded signals This will obviously introduce a linear distortion of the recorded signals, but this is of minor importance in the determination of the presence or absence of response. It should therefore be permissible to reduce the number of repetitions and thus save time

In the investigations which are carried out at present in co-operation with the Institute for Mental Defectives for South East Jutland at Brejning and the State Hearing Rehabilitation Centre in Odense we have chosen to use the evoked potential merely as an indicator of response or non-response to an acoustical signal So far our experience shows that ERA seems to be a useful supplement to the classical audiometric methods On the other hand, the latter methods give when practicable, much quicker and not less accurate results than ERA. In particular ERA has proved very useful in completely unco-operative subjects and has made it possible to determine the hearing acuity in patients with severe mental defects, which has so far been impossible by the classical methods of audiometry

In providing the equipment for this new audiometry it should be kept in mind whether the object is to carry out detailed and accurate studies of the cortical response—which is of great scientific interest, but still of limited clinical value—or just to use the technique as a supplement to existing audiometric methods. In my opinion, the latter object is at present the most profitable and also covers the most urgent demand The equipment needed for this purpose is less complicated and hence less expensive and it will probably be possible to reduce the time required for the test by further technical improvements. Great efforts are made in several institutions in order to achieve this aim

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OTO LARYNGOLOGICA

S U P P L E M E N T U M 262

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HEINZ FERDINAND STUPP

ACTA OTO LARYNGOLOGICA NARVAVÄGEN 14, 115 23 STOCKHOLM

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OTO-LARYNGOLOGICA
SUPPLEMENTUM 262

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ACTA OTO LARYNGOLOGICA

SUPPLEMENTUM 262

Aus der Hals- Nasen- Ohren-Klinik
(Direktor: Professor Dr. A. Meyer zum Gottesberge)
der Universität Düsseldorf

UNTERSUCHUNG DER ANTIBIOTIKASPIEGEL IN DEN INNENOHRFLÜSSIGKEITEN UND IHRE BEDEUTUNG FÜR DIE SPEZIFISCHE OTOTOXIZITÄT DER AMINOGLYKOSIDANTIBIOTIKA

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A. EINLEITUNG

Mit der Entdeckung des Penicillins durch Fleming trat eine entscheidende Wende in der Behandlung der Infektionskrankheiten ein. Es eröffneten sich der Therapie bis dahin ungeahnte Möglichkeiten. Die Isolierung des Streptomycins im Jahre 1943 durch Waksman versprach ein weiterer großer therapeutischer Fortschritt zu werden. Das relativ schmale antibiotische Spektrum des Penicillins fand durch Streptomycin eine wesentliche Verbreiterung. Penicillin und Streptomycin ergänzten sich in geradezu idealer Weise. Mit Recht wird ihre Kombination als das erste antibiotische Breitbandpräparat bezeichnet. Darüberhinaus war Streptomycin auch das erste und bis heute unübertroffene Antibiotikum, das mit Erfolg gegen die größte Geißel der Menschheit, gegen die Tuberkulose eingesetzt werden konnte.

Umso folgenschwerer war daher im Jahre 1945 die Nachricht von Hinshaw und Feldmann über die toxische Wirkung dieser Substanz auf das cochleovestibuläre System. Die Toxizität dieses neuen Antibiotikums überraschte umsomehr, als man gerade erst im Penicillin ein Medikament mit ungewöhnlich günstiger therapeutischer Breite kennengelernt hat. Die Verwendung des Streptomycins wurde auf Grund dieser Eigenschaft erheblich eingeschränkt. Bis heute kann aber auf dieses wertvolle Antibiotikum zur Bekämpfung der Tuberkulose und anderer Infektionen mit gramnegativen Erregern insbesondere bei bestimmten Endocarditisformen nicht verzichtet werden. Zwar gelang es im Laufe der Zeit durch vorsichtigere und genauere, auf den Patienten individuell abgestimmte Dosierungen die toxischen Nebenwirkungen wesentlich herabzusetzen, ohne sie aber ganz beseitigen zu können. Der Arzt sieht sich daher immer wieder vor die verantwortungsvolle Aufgabe gestellt, dieses Antibiotikum trotz seiner Gefahren weiter anzuwenden.

Ähnlich verhält es sich mit allen anderen zur Aminoglykosidgruppe gehörenden Antibiotika, wie Neomycin, Kanamycin, Paromomycin, Framycetin, Gentamycin und einigen weniger bekannten Verbindungen, die in der Folgezeit entwickelt wurden. Sie sind nicht nur chemisch miteinander verwandt, sondern weisen auch sehr ähnliche ototoxische Eigenschaften wie Streptomycin auf. Ihre Toxizität ist sogar noch wesentlich stärker, sodaß ihre therapeutische Anwendung erst recht in Frage gestellt wird bzw. überwiegend auf eine äußerliche Applikation beschränkt bleiben muß. Durch ihre starken antibiotischen Eigenschaften und das außergewöhnlich günstige antibiotische Spektrum würden diese Substanzen sonst eine noch viel größere therapeutische Bedeutung erlangt haben, als es ohnehin schon der

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zuleiten. Darüber hinaus dient sie nach der heute vorherrschenden Meinung den Sinnesepithelien, die keine eigene Blutversorgung besitzen, als Ernährungsmedium.

Die Bedeutung der Endolymphe für die Substrat und O_2-Versorgung unterstreichen u. a. auch die jüngsten Untersuchungen von Lawrence (1965) Durch Messung der Endolymph- und Mikrophonpotentiale konnte gezeigt werden daß eine allgemeine Hypoxämie keinen Einfluß auf die Funktion der Sinneszellen hat Erst die Sauerstoffverarmung in der Endolymphe führt zu einem Zusammenbruch der Mikrophonpotentiale.

Erstaunlicherweise wurde die Bedeutung der Innenohrflüssigkeiten für den ot toxischen Wirkungsmechanismus bis in die jüngste Zeit hinein kaum in Betracht gezogen und bei den Untersuchungen nie berücksichtigt. Ein wesentlicher Grund, warum man sich mit dem Innenohr und seinen Flüssigkeiten so wenig befaßte ist sicher auch in dem sehr komplizierten Bau dieses Organes, das schon die alten Anatomen zu Recht mit dem Namen Labyrinth bedachten, sowie in der geringen Größe und außerordentlichen Empfindlichkeit der feinen Strukturen zu suchen, die für eine Untersuchung nur schwer zugänglich waren.

Die meisten klinischen und experimentellen Arbeiten, deren Zahl kaum noch zu übersehen ist, konzentrierten sich bisher in erster Linie auf die morphologischen und funktionellen Veränderungen an den Sinnesepithelien des Innenohres, dem Cortiorgan der Schnecke, den Christae der Bogengänge und der Macula des Sacculus und Utriculus. Es handelt sich hier bei neben klinischen Beobachtungen fast ausschließlich um histologische histochemische und elektrophysiologische Untersuchungen In der folgenden Übersicht sind die bis heute vorliegenden Befunde und der Stand unserer Kenntnisse über die einzelnen Substanzen der Aminoglykosidgruppe und ihre ototoxischen Schädigungen kurz zusammengefaßt

Fall ist In der praktischen Bedeutung dieser Antibiotika ist sicher auch die Hauptursache zu sehen, warum diese Substanzen bis zum heutigen Tage im Mittelpunkt ausgedehnter toxikologischer Untersuchungen stehen Ziel dieser Bemühungen ist es, die toxische Wirkungsweise aufzudecken und durch Herabsetzung der Toxizitat diese Antibiotikagruppe für einen größeren therapeutischen Anwendungsbereich nutzbar zu machen

Die Aufmerksamkeit der Untersucher konzentrierte sich bisher überwiegend auf allgemeine toxikologische Mechanismen und mögliche chemische Reaktionen dieser Stoffe im Organismus. Zahlreiche Angriffspunkte wer den beschrieben und diskutiert Wir sind aber bis heute noch weit davon entfernt von einer einheitlichen Auffassung sprechen zu können. Vor allem vermag keine der existierenden Theorien über die toxische Wirkung der Streptomycesantibiotika die u E wesentliche und grundlegende Frage zu erklären, warum ausschließlich das Innenohr und die Niere von der Gift wirkung betroffen werden, wahrend die anderen Organe verschont bleiben Erstaunlicherweise fand dieses, für das Verständnis der Streptomycinin toxikation entscheidende Problem der Organspezifitat wie auch Müsebeck (1962) hervorhebt bisher nur wenig Beachtung. Aber gerade in diesem Phänomen so glauben wir ist die eigentliche Ursache für die Ototoxizi tät zu suchen Die Beantwortung dieser Frage wird uns auch einer Erklä rung der toxischen Wirkungsweise naherbringen

Man muß sich zunächst fragen besitzt das Innenohrlabyrinth besondere Merkmale, die eine bevorzugte Schädigung dieses Organes erklären? Wodurch unterscheidet sich das Innenohr von anderen Organen, vor allem von solchen, die eine ähnliche Struktur aufweisen wie z B die Sinnesapparate und das Nervensystem? Histologisch fallen an den Zellen des Innen ohres bzw des N statoakusticus keinerlei Besonderheiten auf die die An nahme einer spezifischen Sensibilität rechtfertigen würden Auch in bio- bzw histochemischer Hinsicht sind keine charakteristischen Unterschiede zu erkennen die uns veranlassen könnten, eine besondere Affinität der toxischen Substanzen zu irgendwelchen chemischen Bausteinen oder Struk turen des Innenohres anzunehmen Derartige Vorstellungen von einer „spezifischen Sensibilität oder „Affinität die immer wieder gerne zur Erklä rung herangezogen werden bleiben daher lediglich hypothetische Erwä gung n für die es bis jetzt keinen Beweis gibt

Auffällig ist jedoch der eigenartige anatomische Aufbau des Cochleo-Vestibularapparates, der im Organismus nicht seinesgleichen hat und dem daher noch am ehesten für das Zustandekommen der spezifischen Ototoxikose eine Bedeutung zuzukommen scheint Charakteristisch ist vor al lem das zweikammerige Flüssigkeitssystem die Peri und Endolymph räume die durch die Reißnersche Membran voneinander getrennt sind Eine weitere Besonderheit des Innenohres ist darin zu sehen daß die Sin neszellen in den Endolymphraum hineinragen und hier in unmittelbarem Kontakt mit der Lymphflüssigkeit stehen Die Endolymphe hat nicht nur die für den Hörvorgang wichtige mechanische Aufgabe Schwingungen fort

praktisch überhaupt nicht bei phylogenetisch höher entwickelten Lebewesen, wo es lediglich zu Gleichgewichtsstörungen kommen soll. Igarashi, McLeod und Graybiel (1966) gingen dieser Frage nach und untersuchten aus diesem Grunde die toxischen Streptomycinwirkungen auf das Hör und Gleichgewichtsorgan an Totenkopfäffchen. Sie fanden hier jedoch die gleichen Veränderungen am Cortiorgan der Schnecke wie an den Christae der Bogengänge, sodaß von einer selektiven Schädigung eines Organes nicht gesprochen werden kann. Auf Grund dieser Befunde warnen die Autoren dringend vor der allzu leichtfertigen Annahme, Streptomycin verursache bei höher entwickelten Lebewesen nur vestibuläre Störungen, aber keine Hörschäden.

Die Entwicklung des Dihydrostreptomycins (DSM) schien zunächst einen Fortschritt für die Streptomycintherapie darzustellen. DSM soll u. a. eine geringere akute Toxizität besitzen, nicht so häufig zu allergischen Reaktionen führen und außerdem stabiler sein als Streptomycin (SM). Bereits nach kurzer Zeit stellte sich aber heraus, daß DSM neben diesen sicher nicht zu unterschätzenden Vorzügen einen großen Nachteil aufweist. DSM ruft beim Menschen viel stärkere Hörschädigungen hervor als SM. Während Gleichgewichtsstörungen in der Regel im weiteren Verlauf durch zentrale Kompensationsvorgänge und auch mit Hilfe der optischen und taktilen Sinnesorgane wieder weitgehend kompensiert werden können, ist der Verlust des Gehörs für den Patienten viel schwerwiegender, da er irreversibel ist und durch kein anderes Organ ersetzt werden kann. Shambaugh *et al.* (1959) empfahlen daher auf die Anwendung des DSM zugunsten des SM zu verzichten, zumal beide Substanzen die gleiche antibiotische Wirksamkeit besitzen. Ähnliche Forderungen erhoben auch Harrison (1949) und Weinstein (1962). Die FDA (Food and Drug Administration) verlangt in ihrem Report vom 3.10.1960, daß DSM nur noch dann verwendet wird, wenn gegen Streptomycin eine Unverträglichkeit besteht. Die Verwendung von DSM in Penicillin-Streptomycin-Zubereitungen wurde für Amerika verboten. In der 17. Auflage der Pharmakopoe der Vereinigten Staaten von Amerika (USP Ausgabe 1965) wurde DSM nicht nur in Kombinationspräparaten, sondern sogar auch als Monoantibiotikum gestrichen. 1964 empfahl auch die Arzneimittelkommission der Deutschen Ärzteschaft DSM nur noch dann zu verordnen, wenn SM nicht vertragen wird. In einer erst kürzlich erschienenen Publikation empfiehlt P. Naumann (1966) DSM nicht mehr anzuwenden und auch SM nur noch bei bestimmten Indikationen, der Tuberkulose und Endokarditis, zu verordnen, sonst aber den antibakteriell wirksameren Antibiotika mit größerer therapeutischer Breite wie Ampicillin und Cephalosporin den Vorzug zu geben. Die Ablehnung des DSM ist nach Ansicht von Zorini (1966) und Mückter (1961 und 1966) nicht überzeugend begründet. Ihrer Meinung nach überwiegen, verglichen mit SM, die Vorteile des DSM bei weitem seine Nachteile.

Die Feststellung, daß eine so geringfügige Veränderung des Streptomycinmoleküls in Dihydrostreptomycin eine umgekehrte und entgegengesetzte

B. BISHERIGE BEFUNDE UND HYPOTHESEN

I. Klinische und experimentelle Befunde zur Ototoxität der Aminoglykosidantibiotika

1. *Streptomycin und Dihydrostreptomycin*

Streptomycin (SM) wurde aus Streptomyces griseus-Kulturen isoliert. Es ist nicht nur das älteste und therapeutisch wichtigste Antibiotikum dieser Gruppe, sondern kann wohl auch als das am meisten untersuchte Antibiotikum überhaupt bezeichnet werden. Nach Mückter (1962) schädigt Streptomycin beim Menschen vor allem das Vestibularissystem (10–30 %) und nur in 2–3 % den cochleären Apparat. Da Streptomycin bevorzugt den Gleichgewichtsapparat zu schädigen scheint, wurde es auch zur Ausschaltung des Vorhofbogengangsystems bei peripher bedingten Gleichgewichtsstörungen, z. B. bei der Menière'schen Krankheit, verwendet. Weder Fowler (1948) noch Hamberger *et al.* (1949), Rüedi (1951) oder Hanson (1951) sahen bei dieser Behandlung wesentliche Hörstörungen. Andere Untersucher beobachteten allerdings stärkere Hörschäden und warnten deshalb vor der kritiklosen Anwendung des Streptomycins.

Die zahlreichen klinischen Befunde fanden in tierexperimentellen Untersuchungen ihre Bestätigung. Die Verhältnisse scheinen jedoch beim Tier von Spezies zu Spezies verschieden zu sein. Beim Meerschweinchen und der Katze soll Streptomycin das Hörorgan sogar wesentlich stärker schädigen als den Bogengangsapparat (Hawkins *et al.*, 1947; Tyberghein, 1962; Mückter, 1962). Bei der Durchsicht der Literatur stößt man jedoch auf viele einander widersprechende Befunde. Müsebeck (1961) z. B. stellte unter Streptomycin beim Meerschweinchen genau das Gegenteil fest, nämlich daß der Gleichgewichtsapparat stärker betroffen ist als die Cochlea. Hör- und Gleichgewichtsstörungen wurden bei der Katze außerdem von Keller *et al.* (1955), bei Hunden von Molitor *et al.* (1946, 1948 und 1950), ferner bei Kaninchen von Hawkins *et al.* (1951) und bei Mäusen und Ratten von Caussé *et al.* (1948 und 1949), von Keller *et al.* (1955), von Brigham und Nielsen (1958) sowie von Lagler *et al.* (1960) und zahlreichen anderen Autoren beschrieben. Tauben zeigten einen vollständigen Verlust des Nachnystagmus, ohne daß dabei das Flugvermögen beeinträchtigt wurde. Dagegen konnten bei Hühnern unter Streptomycin erhebliche Gleichgewichtsstörungen mit ataktischen Erscheinungen beobachtet werden. Nach Weitnauer *et al.* (1957) reagieren auch Fische mit Seiten- und Bauchlage.

Im allgemeinen wird angenommen, daß Streptomycin Hörschädigungen ausschließlich bei niederen Tieren hervorruft, dagegen nur selten der

praktisch überhaupt nicht bei phylogenetisch höher entwickelten Lebewesen, wo es lediglich zu Gleichgewichtsstörungen kommen soll. Igarashi, McLeod und Graybiel (1966) gingen dieser Frage nach und untersuchten aus diesem Grunde die toxischen Streptomycinwirkungen auf das Hör- und Gleichgewichtsorgan an Totenkopfäffchen. Sie fanden hier jedoch die gleichen Veränderungen am Cortiorgan der Schnecke wie an den Christae der Bogengänge, sodaß von einer selektiven Schädigung eines Organes nicht gesprochen werden kann. Auf Grund dieser Befunde warnen die Autoren dringend vor der allzu leichtfertigen Annahme, Streptomycin verursache bei höher entwickelten Lebewesen nur vestibuläre Störungen, aber keine Hörschäden.

Die Entwicklung des Dihydrostreptomycins (DSM) schien zunächst einen Fortschritt für die Streptomycintherapie darzustellen. DSM soll u. a. eine geringere akute Toxizität besitzen, nicht so häufig zu allergischen Reaktionen führen und außerdem stabiler sein als Streptomycin (SM). Bereits nach kurzer Zeit stellte sich aber heraus, daß DSM neben diesen sicher nicht zu unterschätzenden Vorzügen einen großen Nachteil aufweist. DSM ruft beim Menschen viel stärkere Hörschädigungen hervor als SM. Während Gleichgewichtsstörungen in der Regel im weiteren Verlauf durch zentrale Kompensationsvorgänge und auch mit Hilfe der optischen und taktilen Sinnesorgane wieder weitgehend kompensiert werden können, ist der Verlust des Gehörs für den Patienten viel schwerwiegender, da er irreversibel ist und durch kein anderes Organ ersetzt werden kann. Shambaugh *et al.* (1959) empfahlen daher auf die Anwendung des DSM *zugunsten* des SM zu verzichten, zumal beide Substanzen die gleiche *antibiotische* Wirksamkeit besitzen. Ähnliche Forderungen erhoben auch Harrison (1960) und *Weinstein* (1962). *Die FDA* (Food and Drug Administration) verlangt in ihrem Report vom 3.10.1960, daß DSM *nur* noch dann verwendet wird, wenn *gegen Streptomycin* eine Unverträglichkeit besteht. Die Verwendung von DSM in Penicillin-Streptomycin-Zubereitungen wurde für Amerika verboten. In der 17. *Auflage der Pharmakopoe* der Vereinigten Staaten von Amerika (USP *Ausgabe* 1965) wurde DSM nicht *nur* in Kombinationspräparaten, sondern sogar auch als Monoantibiotikum *gestrichen*. 1964 empfahl auch die Arzneimittelkommission der Deutschen Ärzteschaft, DSM nur noch dann zu verordnen, wenn SM nicht vertragen wird. In einer erst kürzlich erschienenen Publikation *empfiehlt P.* Naumann (1966) DSM nicht mehr anzuwenden und auch SM *nur* noch bei bestimmten Indikationen, der Tuberkulose und Endokarditis, zu verordnen, sonst aber den antibakteriell wirksameren Antibiotika mit *größerer therapeutischer* Breite wie Ampicillin und Cephalosporin *den* Vorzug zu geben. Die Ablehnung des DSM ist nach Ansicht von *Zorlal* (1966) und Möckter (1961 und 1966) nicht überzeugend begründet. Ihrer Meinung nach überwiegen, verglichen mit SM, die Vorteile des DSM bei weitem seine Nachteile.

Die Feststellung, daß eine so geringfügige Veränderung des Streptomycinmoleküls in Dihydrostreptomycin *eine* umgekehrte und entgegengesetzte

toxische Wirkung haben soll, stellt ein interessantes Phänomen dar, wofür es bis heute keine Erklärung gibt. Es gilt zwar allgemein die Regel, daß SM Gleichgewichtsstörungen und DSM Hörschädigungen verursacht. Dieses gegensätzliche Verhalten von SM und DSM sollte aber, wie eben schon am Beispiel des SM gezeigt wurde, nicht überbewertet werden. Wenn man die in der Literatur mitgeteilten widerspruchsvollen Befunde berücksichtigt, erscheint eine vorsichtigere Beurteilung angeraten. Besser wäre es zumindest, da meistens früher oder später bei beiden Substanzen sowohl cochleo- als auch vestibuläre Störungen auftreten, von einer bevorzugten Schädigung des Vestibularapparates oder des Cortiorganes zu sprechen.

Durch Reinigung der Streptomycinpräparate, insbesondere von Lösungsrückständen (Methylalkohol) und Metallionen (Calcium), konnten die toxischen Nebenwirkungen erheblich vermindert werden. Kimmerle und Gösswald (1956) sowie Kuschinski, Lüllmann und Pracht (1960) vermochten bei Ratten selbst nach wochenlanger Behandlung keine SM- und DSM-Schädigungen nachzuweisen. Kimmerle und Gösswald gingen sogar soweit, alle bisherigen Befunde und Mitteilungen über toxische Hörstörungen nach Dihydrostreptomycin nicht nur bei der Ratte, sondern auch bei anderen Tieren und sogar beim Menschen in Frage zu stellen. Im Gegensatz hierzu berichten aber zahlreiche andere Untersucher wie Courvoisier und Leau (1956), *Ducrot, Leau und Cosar* (1958), *Osterberg et al.* (1956), Beccari, Cuida und Mollnengo (1957), Maeda *et al.* (1957), Takeuchi *et al.* (1958) sowie Tisch, Huftalen und Dickison 1958 über deutliche Hörschäden bei Ratten nach DSM.

Besonders aufschlußreich sind angesichts dieser widersprechenden Befunde die von Mahady und Mitarbeitern in den Jahren 1953 und 1956 unter gleichen Bedingungen durchgeführten vergleichenden Untersuchungen mit allen handelsüblichen DSM-Präparaten und hochgereinigtem kristallinem DSM-Sulfat. Die beiden Präparate unterschieden sich hierbei nicht in ihren ototoxischen Eigenschaften. Es muß daher in Übereinstimmung mit Mückter angenommen werden, daß die spezifisch ototoxische Wirkung nicht auf Verunreinigungen zurückzuführen ist, sondern, wie Molitor bereits im Jahre 1948 vermutete, wahrscheinlich ausschließlich auf dem SM-Molekül und seinen Abbauprodukten beruht. Durch die Reinigung des Streptomycins gelang es allerdings, darin stimmen alle Untersucher überein, die allergischen Nebenwirkungen, die zu den häufigsten Komplikationen der Streptomycintherapie zählten, praktisch vollständig zu beseitigen.

Widersprechende Angaben finden sich auch hinsichtlich der Lokalisation der Streptomycinschädigungen. Die von Winston, Lewey, Parenteau, Marden und Cramer (1948) festgestellten Veränderungen an den Purkinjezellen, am Flocculus und Nodulus, am Deiterschen Kern und Nucleus dentatus des Kleinhirns sowie im medialen Vestibulariskern sprechen für einen zentralen Angriffspunkt des SM. Die Ursache hierfür glauben die Untersucher in einer erhöhten Permeabilität der Hirnschranke sehen zu

können. Winston und Mitarbeiter konnten zeigen, daß die Bluthirnschranke unter SM für Trypanblau durchlässig wird. Für die Annahme eines zentralen Angriffspunktes würden auch die Befunde von Floberg, Hamberger und Hyden (1949) sprechen, die unter SM eine Abnahme des Nucleinsäuregehaltes in den Zellen des Ganglion vestibulare des Meerschweinchens beobachteten. Escher (1949) berichtete außerdem über Ganglienzelluntergänge im Ganglion triangulare und Nucleus angularis. Secondi (1954) sah auch Schädigungen an den Vestibulariskernen, den Purkinjezellen und im Hippocampus. Christensen, Hertz, Riskaer und Vraa Jensen (1950) unterzogen nicht nur die zentralen Bahnen des N. statoakusticus, sondern auch den peripheren Sinnesapparat einer histologischen Untersuchung. Sie fanden eine Degeneration der rhombencephalen Cochlearis- und Vestibulariskerne, des Ganglion vestibulare sowie der Purkinjezellen des Kleinhirns. Die Sinnesepithelien des Cortiorgans und des Vestibularapparates schienen dagegen intakt zu sein. Bei Untersuchungen, die einige Jahre später von der gleichen Forschergruppe (Riskaer Christensen, Petersen und Weidman, 1956) durchgeführt wurden, stellte man jedoch auch periphere Schädigungen am Labyrinth fest, die aber nur gering sein sollen gegenüber den Veränderungen am ZNS.

Im Gegensatz zu den oben aufgeführten Untersuchungsergebnissen kam Greven (1953) auf Grund histologischer Untersuchungen zu dem Schluß, daß SM auf die zentralen Bahnen und Umschaltstellen des N. Statoakusticus keinen Einfluß hat. Auch Caussé (1949) beobachtete bei Mäusen nur periphere Schädigungen an den Christae ampullares, den Maculae staticae und am Cortiorgan, während die cochleovestibulären Kerngebiete keine Zeichen einer Schädigung aufwiesen. Eine toxische Wirkung des Streptomycins auf die peripheren Sinneszellen wurde ferner von Graf (1951) Berg (1951) Rüedi, Furrer Luthy Nager und Tschirren (1952) Hawkins, Wolcott und O'Shonny (1956–1957) Catalano und Madonia (1956) Neumann und Neubert (1958) und vielen anderen und in jüngster Zeit noch von Holde Hata und Hando (1966) sowie Igarashi, McLeod und Graybiel (1966) beschrieben.

Müsebeck und Schätzle (1963) und Müsebeck (1963, 1964) sahen allerdings die ersten Zeichen einer Schädigung nicht an den Sinneszellen, sondern vielmehr an den Mitochondrien der sog. sekretorischen Epithelien des Innenohres. Die Veränderungen an den Mitochondrien der Sinneszellen treten, wie sich histochemisch nachweisen ließ, erst später auf und sollen sekundärer Natur sein.

Bei diesem kurzen Überblick fällt auf daß sich Mitteilungen über toxische Streptomycinwirkungen auf das ZNS vor allem in der älteren Literatur finden. Die weitaus überwiegende Zahl der Berichte, insbesondere aus der jüngsten Zeit, spricht für eine primär periphere Schädigung.

Eckel und Altenburger (1960) vermuten die Ursache für die verschiedenen Befunde in den unterschiedlichen Dosierungen. Sie glauben, daß in einem mittleren Dosisbereich ausschließlich periphere Schädigungen auf

treten und nur durch sehr hohe bereits zu einer Allgemeintoxikation führende Streptomycinmengen Veränderungen im Kerngebiet hervorgerufen werden Diese Auffassung wird heute allgemein vertreten Dennoch machten Neumann und Neubert (1958) auf das Mißverhältnis zwischen den peripheren morphologischen Befunden und den ausgeprägten funktionellen Ausfallserscheinungen aufmerksam Sie nehmen aus diesem Grunde an daß für die Hör und Gleichgewichtsstörungen neben peripheren auch zentralnervöse SM-Schädigungen verantwortlich gemacht werden müssen Die Frage bleibt jedoch unbeantwortet ob die zentralen Veränderungen ebenfalls primärer Natur oder möglicherweise nur sekundär bedingt sind Engström und auch Kohonen (1965) äußerten die Vermutung, daß es sich bei den Veränderungen im Nervensystem um sekundäre Degenerationserscheinungen der zugeordneten Nervenbahnen handelt Eine langsam fortschreitende Degeneration würde auch den meist erst sehr spät auftretenden und oft nach Absetzen der Therapie noch über eine lange Zeit langsam fortschreitenden Funktionsausfall erklären Zeitlich gesehen treten in der Regel die ersten Zeichen einer Gleichgewichtsstörung wenige Wochen nach Behandlungsbeginn in Erscheinung, während sich eine Schwerhörigkeit häufig sehr viel später oft erst nach einer Latenzzeit von wenigen Tagen bis zu 6 oder sogar 7 Monaten nach Absetzen der Therapie bemerkbar macht (Shambaugh *et al* 1959 Harrison, 1959–60 Rossi *et al* 1961 Mückter 1961)

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Lindsay und Mitarbeiter konnten die Felsenbeine eines an Endocarditis verstorbenen Patienten untersuchen, der mit 18 g Neomycin behandelt worden war und dabei ertaubte. Sie fanden ebenfalls keine Veränderungen des vestibulären Sinnesepithels. Auch im Bereich der Stria vascularis waren keine Schädigungen zu erkennen, dagegen zeigten sich ausgedehnte Zerstörungen bzw ein vollständiges Verschwinden der Haarzellen, insbesondere der inneren Zellen.

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Ein Vergleich der ototoxischen Wirkungen der einzelnen basischen Streptomyces-Antibiotika zeigte daß Neomycin die weitaus stärksten ototoxischen Schädigungen hervorruft (Hawkins, 1952 Hawkins und Lurie, 1953 Courvoisier und Leau, 1956) Tyberghein (1962) untersuchte auch die verschiedenen Salze des Neomycins, die Pantothenatkomplexe und die Sulfitverbindung. An der Abnahme der Mikrophonpotentiale stellte er fest 1 8 Neomycin die schwersten Haarzellenschädigungen von allen Streptomyces-Antibiotika verursacht. Die Toxizität des Neomycins konnte auch

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durch Zusatz von Panthenol nicht herabgesetzt werden Die besonders ausgeprägte Ototoxizität des Neomycins hebt auch Finland (1961) in seiner Monographie hervor

Zu dem gleichen Ergebnis kamen Riskaer und Mitarbeiter (1956) die den toxischen Einfluß des Neomycins auf die Haarzellen die Stria vascularis und die neuralen Elemente mit Streptomycin, Viomycin und Polymyxin B verglichen Neomycin erwies sich hierbei am stärksten toxisch. Sie konnten ebenfalls unter Neomycin keine Schädigungen am Vestibularapparat feststellen

Friedmann und Bird (1961) führten ihre Untersuchungen an der Otocyste von Hühnerembryonen durch und kamen hier zu der gleichen Feststellung Neomycin und Kanamycin weisen zwar im Prinzip ein ähnliches Schädigungsbild auf die Veränderungen unter Neomycin waren aber viel ausgeprägter als bei Kanamycin

3 *Kanamycin*

Kanamycin wurde 1957 von Umezawa aus dem Filtrat einer Kultur von Streptomyces strain, der Umezawa den Namen Streptomyces kanamyceticus gab, isoliert Sowohl in chemischer Hinsicht als auch in seinem antibiotischen Wirkungsspektrum gleicht Kanamycin dem Neomycin.

Es überraschte daher nicht weiter als bald eine große Zahl wissenschaftlicher Arbeiten über die nephro- und ototoxischen Wirkungen des Kanamycins erschien (Bunn *et al* 1958 White, 1958 Ichikawa, 1958 Donomae 1958 Finegold *et al* 1958 March 1959 Frost *et al.*, 1958/59 und 1960 Naunton and Ward, 1959 Lustberg und Hamburger 1959 Lecca *et al.*, 1959 Bouche *et al* 1960 Alfthan *et al.*, 1962 Haapanen, 1963 Degreef 1964 Marseillan, 1965)

Ähnlich wie bei Neomycin stehen auch bei Kanamycin Hörschädigungen im Vordergrund, die zuerst die hohen Frequenzen betreffen. Vestibuläre Störungen wurden dagegen nur in seltenen Fallen beschrieben so z. B von Matz (1965) Besonders schwere Ototoxikosen beobachtete man bei Nierenschädigungen verschiedener Genese (Ichikawa, 1958 White 1958 Naunton und Ward 1959 Lecca, Terry Maggiolo und Morales, 1959)

Im Tierexperiment konnten mit Hilfe elektrophysiologischer Methoden Hörschadigungen von Hawkins (1959) Tyberghein (1962) Owada (1962) sowie Plattig und Keidel (1965) nachgewiesen werden Hawkins unterzog die Tiere außerdem einer histologischen Untersuchung Er fand bei Katzen Meerschweinchen und weniger ausgeprägt bei Ratten, Schädigungen der äußeren Haarzellen, vor allem in den basalen Windungen wahrend die inneren Haarzellen in allen Windungen fehlten Es war aber auch eine Verringerung der Ganglienzellen und Nervenfasern in der Lamina spiralis ossea feststellbar Dagegen erwiesen sich das Ganglion spirale und Neuroepithel der Cristae ampullares beim Meerschweinchen als normal

Einen Verlust an Ganglienzellen und Haarzellschädigungen in den un

teren Windungen der Meerschweinchencochlea beschrieben ebenfalls Catalano und Mitarbeiter (1961)

Ähnliche histologische Befunde erhoben Ward und Fernandez (1961) Darüber hinaus stellten sie aber auch Veränderungen im Kleinhirn und Hirnstamm, sowie eine Verminderung nicht nur der Ganglienzellen, sondern auch der Fasern des Hörnerven fest

Mesolella und Costa kamen 1962 im wesentlichen zu dem gleichen Ergebnis. Sie heben jedoch hervor daß die Schädigungen im Bereich des ZNS und des Ganglions nur gering waren, verglichen mit den ausgeprägten Veränderungen am peripheren Sinnesapparat. Im Gegensatz zu Hawkins sahen sie auch Schädigungen an den Sinneszellen des Gleichgewichtsapparates.

Darrouzet und de Lima Sobrinho (1962) fielen neben Zerstörungen der äußeren Haarzellen in den Basalwindungen außerdem leichte Veränderungen an den Stützzellen auf. Reddy und Igarashi (1962) sind sogar der Meinung, daß die Stützzellen besonders empfindlich sind und als erste geschädigt werden, während die Haarzellschädigungen später nachfolgen sollen.

Mit Hilfe der Häutchenpräparation nach Neubert (1950) untersuchten Beck und Krahl (1962) die Kanamycinschädigungen an der Meerschweinchencochlea. Sie stellten zunächst als 1 Zeichen einer toxischen Störung eine Unregelmäßigkeit an den Kernen der äußeren Haarzellen und zwar in der 1 innersten Reihe der unteren Schneckenwindungen *fest, die* spä ter auf die 2. und 3. Reihe der äußeren Haarzellen *übergreift. Auch* Müsebeck sah regelmäßig, daß die *1 Reihe* der äußeren Haarzellen am empfindlichsten geschädigt wurde, die Störungen in der 2. und 3. Reihe dagegen *deutlich* geringer waren, während die inneren Haarzellen relativ widerstandsfähig erschienen.

Neben den Sinnesepithelschädigungen ruft Kanamycin nach den Untersuchungen *von Beck und Krahl* auch an den *Epithelzellen der Stria vas*cularis und den Deitersschen Zellen ähnliche Veränderungen hervor wie sie schon unter Streptomycin (Müsebeck und Schätzle) und Neomycin (Rüedi) beschrieben wurden. Die *stärksten Schäden fanden* auch sie bemerkenswerterweise in der oberflächlichsten, *dem* Endolymphraum zugewandten Epithelschicht. Darüber hinaus fanden Beck und Krahl auch zentrale Veränderungen an den Ganglienzellen, vor allem im Kerngebiet. Das Ausmaß der Schädigung nimmt, wie sich *histochemisch* zeigen ließ, vom peripheren Sinnesapparat über *die Kerngebiete* hin zu den übergeordneten Hirnabschnitten deutlich ab.

Ardouin, Saft und Jobard (1963) beobachteten fast ausschließlich eine Schädigung der äußeren Haarzellen, insbesondere der unteren Windungen. Dagegen stellten sich die inneren *Haarzellen, die* Stützzellen und neuralen Elemente bei ihren Untersuchungen *unauffällig* dar

Neue Erkenntnisse brachten die kombinierten licht und elektronenmikroskopischen Untersuchungen Farkashidys, Blacks und Briants (1963) Be-

sonders bemerkenswert ist im Rahmen unserer Betrachtungen der Schluß, den Farkashidy und seine Mitarbeiter aus ihren Untersuchungen ziehen. Es fiel ihnen auf, daß die ersten Degenerationszeichen mit Verklumpungen der Mitochondrien und des endoplasmatischen Retikulums stets im supranukleären, dem Endolymphraum zugekehrten Bereich der Zelle auftraten. Sie äußern daher den Verdacht, daß die Kanamycinschädigung vom Endolymphraum aus erfolgt, wo eine besonders hohe Konzentration des Antibiotikums vermutet wird.

Die gleichen, im Tierexperiment beobachteten Veränderungen im Bereich der basalen Windungen wurden auch in den 3 bis heute untersuchten Fällen beim Menschen beschrieben (Benitez, Schuknecht und Brandenburg, 1962; Jorgensen und Schmidt, 1962). Matz, Wallace und Ward (1965) hatten die Gelegenheit, ein menschliches Felsenbein nach einer kurzfristigen Kanamycinbehandlung, die zu einer Taubheit und einem Ausfall der kalorischen Erregbarkeit der Bogengangsapparate geführt hatte, histologisch zu untersuchen. Ein Vergleich mit experimentell erzeugten Kanamycinschädigungen am Innenohr des Meerschweinchens führte die Untersucher zu der Feststellung, daß kein Unterschied zwischen der Histopathologie der menschlichen Ototoxikose und der tierexperimentellen Innenohrintoxikation besteht. Erstaunlicherweise fanden die Untersucher trotz des klinisch eindeutigen Ausfalls der Vorhofbogengangsfunktion keine morphologisch faßbaren Veränderungen an den peripheren Vestibularapparaten. Sie vermuten daher die Ursache für die Gleichgewichtsregulationsstörung in den übergeordneten Zentren des ZNS.

4. Viomycin, Framycetin, Paromomycin und Gentamycin

Zur Gruppe der Aminoglykosidantibiotika zählen außer Streptomycin, Neomycin und Kanamycin noch Viomycin, Framycetin, das Vancomycin und Paromomycin, auch Aminosidine (Gabromycin*) genannt, sowie das Gentamycin. Sie sollen hier nur der Vollständigkeit halber kurz erwähnt werden. Über ihre Pharmakologie und Toxikologie ist bis heute nur wenig bekannt.

Viomycin aus Streptomyces puniceus, das vor allem zur Behandlung der Tuberkulose Anwendung findet, ruft ebenfalls, wie Werner und Mitarbeiter 1951 erstmals berichteten, Innenohrschädigungen und zwar in 1. Linie Gleichgewichtsstörungen hervor. Weniger ausgeprägt sind bei Viomycin die Hörschädigungen. Es folgten noch weitere klinische Mitteilungen über die Toxizität des Viomycins von Schaffeld *et al.* (1951), Hitts *et al.* (1952), Tucker *et al.* (1954) sowie Edge *et al.* (1960). Nach Daly und Cohen ist Viomycin gegen Tuberkelbazillen nur 1/3 so wirksam wie Streptomycin, dafür aber deutlich toxischer als dieses. Die Toxizität soll jedoch nicht ganz so ausgeprägt sein wie bei Kanamycin.

Über *Framycetin*, das aus Streptomyces lavendulae gewonnen wird, liegen bisher nur wenige Untersuchungsergebnisse vor. Massenat und Déroche

(1954) sahen bei ihren Patienten starke toxische Nebenwirkungen auf Ohren und Nieren.

Tierexperimentell gelang es erstmals Kohonen (1965) Schädigungen der äußeren Haarzellen durch Framycetin nachzuweisen. Hinsichtlich seiner Ototoxizität scheint es dem Neomycin nur wenig nachzustehen.

Über das Antibiotikum *Aminosidin* das chemisch mit Paromomycin identisch ist und von Canevazzi und Scotti (1959) aus Streptomyces chrestomyceticus isoliert wurde berichtete erst kürzlich Marsellian (1965) Ein Vergleich mit Kanamycin ergab, daß Aminosidin sowohl gemessen am Gewichtsabfall der Versuchstiere als auch hinsichtlich seiner hörschädigenden Wirkung etwas toxischer ist als Kanamycin.

An der Ratte und Katze (Arcamone *et al* 1959) und am Meerschweinchen (Manzo und Mea, 1961) konnten sowohl cochleo- als auch vestibulotoxische Effekte des Aminosidins nachgewiesen werden. Während beim Meerschweinchen die Hörschädigungen im Vordergrund standen, zeigten Katzen vor allem vestibuläre Symptome

Gentamycin (Refobacin®) wurde erst 1963 von der Arbeitsgruppe M. J Weinstein aus den Fermentationsansätzen bis dahin noch unbekannter Streptomycesarten, Micromonospora purpurea und M echinospora, gewonnen. Nach Wersäll und Lundquist weist es die weitaus stärksten vestibulo- und cochleotoxischen Erscheinungen von allen Aminoglykosidantibiotika auf besitzt aber andererseits besonders hervorragende antibiotische Eigenschaften, z. B gegen therapieresistente Staphylokokken, Pseudomonas aeruginosa und andere Problemkeime Seine starke Ototoxizität wird durch eine 10fach höhere antibiotische Wirksamkeit mehr als aufgewogen, sodaß nur 1/10 der sonst üblichen Dosen verabreicht werden muß Holz und Soda (1967) verglichen antibiotisch gleichwertige Dosen von Streptomycin, Neomycin und Gentamycin Sie stellten fest, daß Gentamycin *in dieser Dosierung* sogar weniger toxisch ist als Streptomycin.

Zusammenfassend läßt sich von den Antibiotika der Aminoglykosidgruppe folgendes sagen

Die toxischen Schädigungen weisen bei allen Substanzen die gleichen Grundzüge auf Übereinstimmend mit *Müsebeck*, Kohonen und vielen anderen kann als wahrscheinlich angenommen werden, daß der primäre Schädigungsort der basischen Streptomycesantibiotika im peripheren Sinnesorgan zu suchen ist Den Beweis hierfür lieferten schon die frühen Untersuchungen von Causse und Berg und erst recht die mit verbesserten Methoden durchgeführten Untersuchungen der letzten Jahre

Die Schädigung der einzelnen *Abschnitte* und Zellen des Innenohres erfolgt in einer bestimmten gesetzmäßigen Reihenfolge Dieses sog Schädigungsmuster scheint ebenfalls bei allen Antibiotika das gleiche zu sein

Beck und Krahl (1962) nahmen zunächst an, daß die bevorzugte Schädigung der basalen Haarzellen auf einer langsameren Strömungsgeschwindigkeit des Blutes in den unteren Schneckenwindungen beruht Diese Vorstellung widerlegte Kohonen (1965) indem er zeigte, daß z. B. die inneren

² ® ... [illegible]

Haarzellen im Gegensatz zu den äußeren Zellen überwiegend in den apikalen Abschnitten eine besondere Empfindlichkeit aufweisen. Mit Hilfe der Phasenkontrastmikroskopie und der von Engström entwickelten Oberflächenpräparationstechnik stellte Kohonen eine unterschiedliche Nervenversorgung der einzelnen Haarzellen fest. Die *Verteilung der reich granulierten* Nervenendigungen ließ eine Gesetzmäßigkeit erkennen. Die Zahl der granulierten Nervenendigungen nimmt z. B. bei den äußeren Haarzellen von der Basis zur Spitze hin und von der inneren zur äußeren Reihe hin ab. In den gleichen Richtungen, radial und linear zur Schneckenspitze, verlauft auch die Degeneration der Haarzellen bei der Intoxikation. Nach Kohonen ist die Empfindlichkeit der Haarzellen gegenüber den toxischen Antibiotika direkt *proportional der Zahl ihrer Nervenendigungen*.

Koide, Hata und Hando (1966) kamen auf Grund histochemischer Untersuchungen zu einem ähnlichen Ergebnis, wenn man unterstellt, daß die Innervation in einem engen Verhaltnis zur Funktion und damit zur Stoffwechselintensität der Zelle steht. Auch bei diesen Untersuchungen fiel eine Korrelation zwischen der Stoffwechselaktivität der Haarzellen und ihrer Vulnerabilität auf. Die histochemisch durch ihren besonders hohen Succinaldehydrogenasegehalt *sich auszeichnenden äußeren Haarzellen wiesen* regelmäßig die ersten Veränderungen auf.

Diese Schadigungsfolge ist aber nicht nur charakteristisch für Streptomycin und die übrigen Antibiotika mit Oligosaccharidstruktur, sondern gilt nach den Untersuchungen Koides und seiner Mitarbeiter genau so für Chloramphenicol und Chinin. Voraussetzung ist nur, daß die Substanzen unmittelbar an das Innenohr herangebracht werden. Koide gab die toxischen *Stoffe direkt in die Paukenhöhle vor die dünne Membran des runden* Fensters, damit sie von hier aus in hoher Konzentration in das Innenohr diffundieren können. Sogar O_2-Mangel, Ultraschall und Hochfrequenzstrom können, wie Beck und Michler (1960) feststellten, das gleiche Schadigungsbild wie die Streptomyces-Antibiotika hervorrufen.

Nicht nur die Sinnesepithelien, sondern fast alle Zellen des Innenohres wie die Ganglienzellen, die Stützzellen des Cortiorgans oder die Epithelien der *Stria vascularis* lassen früher oder spater — einige Untersucher glauben sogar noch vor den Haarzellen — Zeichen einer Schädigung erkennen. Dies Tatsache spricht dafür, daß die Spezifität der Intoxikation nicht, wie immer wieder behauptet wird, auf einen einzigen Zelltyp, die Haarzellen, denen eine spezifische Empfindlichkeit zugeschrieben wird, beschränkt ist, sondern vielmehr *auf das ganze Innenohrorgan zutrifft*.

Mit Hilfe morphologischer und funktioneller Untersuchungsmethoden gelang es zwar, den Angriffspunkt und die Schadigungsfolgen zu bestimmen. Es muß jedoch Müsebeck zugestimmt werden, wenn er feststellt, daß die morphologische Technik ebenso wenig wie die funktionellen Prüfungen irgend eine Aussage über den eigentlichen Wirkungsmechanismus zulassen, ja, daß sie teilweise sogar zu Fehlbeurteilungen geführt haben.

II Zur Pharmakologie und Toxikologie der ototoxischen Streptomyces-Antibiotika

1 Die Struktur der toxischen basischen Antibiotika

Abraham und Newton machten auf dem IV Internationalen Kongreß für Biochemie den Vorschlag, die Antibiotika nach chemisch strukturellen Gesichtspunkten einzuteilen. Die toxischen Streptomycesantibiotika Strept mycin, Neomycin, Kanamycin, Paromomycin und einige weniger bekannte Verbindungen werden in dieser Einteilung als eine geschlossene Gruppe zusammengefaßt, die durch die Struktureinheit Zucker gekennzeichnet wird In der Literatur wird auch häufig von den Antibiotika der Oligosaccharidgruppe oder den Aminoglykosidantibiotika gesprochen.

Andere Autoren bevorzugen die Bezeichnung „basische Streptomycesantibiotika (Mückter 1961) nicht nur weil die stark basische Eigenschaft ein charakteristisches Merkmal der ot toxischen Antibiotika darstellt, sondern weil darüber hinaus der Basizität auch eine besondere Bedeutung für die toxische Wirkungsweise beigemessen wird.

Sämtliche Streptomycessubstanzen dieser Gruppe besitzen als gemeinsames Strukturmerkmal basische Hexosen, basische Cyclite, ringständige basische Gruppen und primäre Aminogruppen.

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Mit Hilfe morphologischer und funktioneller Untersuchungsmethoden gelang es zwar den Angriffspunkt und die Schädigungsfolgen zu bestimmen Es muß jedoch Müsebeck zugestimmt werden wenn er feststellt daß die morphologische Technik ebenso wenig wie die funktionellen Prüfungen irgend eine Aussage über den eigentlichen Wirkungsmechanismus zulassen ja, daß sie teilweise sogar zu Fehlbeurteilungen geführt haben

lamin ergaben. Bei den antagonistisch wirkenden, depolarisierenden Substanzen vom Typ des Succinylcholins fand sich entsprechend eine Abschwächung der relaxierenden Wirkung des Streptomycins.

Während der akute Vergiftungsmechanismus weitgehend erforscht zu sein scheint, sind unsere Kenntnisse über die spezifisch oto- und nephrotoxische Wirkung noch sehr lückenhaft und unsicher. Nach Möckters Ansicht ist die für die akute Vergiftung offenbar wesentliche Verminderung des Calciums bzw. seiner Ionisation für die spezifische Intoxikation wahrscheinlich ohne Bedeutung. Sie könnte eher mit den antienzymatischen Erscheinungen, wie sie bei der chronischen bzw. semichronischen Vergiftung beschrieben worden sind, in Zusammenhang gebracht werden.

Schon im Jahre 1949 wies Umbreit darauf hin, daß SM auf den sowohl für die Bakterienzelle als auch für die Zellen des Organismus gleichermaßen wichtigen Krebscyclus einen Einfluß hat. SM soll in die Reaktion Brenztraubensäure-Oxalessigsäure und damit in die energetische Versorgung zur Erhaltung der Struktur und Funktion der Zelle eingreifen.

Hauptenergiequelle für die Zelle sind die Kohlehydrate, die im Organismus stufenweise unter Mitwirkung von Enzymen abgebaut werden. Der Abbau erfolgt vom Glycogen bzw. der Glucose ausgehend durch Phosphorylierungsvorgänge über Triosephosphate bis zur Brenztraubensäure. Diese wird ebenso wie die Abbauprodukte des Eiweißes und der Fette über eine mehrstufige Reaktion, die über Thioester zur Bildung von *Acetyl-Coenzym A* führt, in den Zitronensäurecyclus eingeschleust. Hier erfolgt der weitere Abbau durch Oxydation und stufenweise Freisetzung der Energie.

Keller, Krüpe, Sous und Möckler (1955) vermuteten bereits die Ursache für die Streptomycinschädigung in einer Störung des Coenzym-A Systems. Diese Vorstellung fand durch die Untersuchungen von Mascitelli-Coriandoli (1902) eine experimentelle Stütze. Mascitelli-Coriandoli konnte unter SM, DSM und Neomycin in verschiedenen Organen, vor allem in den Mitochondrien eine Herabsetzung des Coenzym-A-Gehaltes nachweisen. Auf die Verminderung des Coenzym-A in der Nebennierenrinde ist nach seiner Ansicht auch die gestörte Corticosteroidsynthese zurückzuführen.

Die Hemmung der Nebennierenrindenfunktion läßt sich, das sei hier am Rande bemerkt, aber auch auf andere Weise erklären. Sie könnte ebenso gut durch eine direkte Konkurrenz der basischen Streptomycesantibiotika mit basischen Makromolekülen wie ACTH erklärt werden, eine Auffassung, die vor allem von Higginbotham und Dougherty (1957) vertreten wird.

Auf welche Weise Streptomycin das Coenzym A zu beeinflussen vermag, zeigen die Untersuchungen Liebsteins und Gilfillans (1951). Danach hemmt SM die Synthese der Pantothensäure, die einen wichtigen Baustein des Coenzym A darstellt. Untersuchungen an Saccharomycesarten ergaben, daß SM die Verbindung von Pantoyllacton mit β-Alanin verhindert.

Andererseits muß hier aber auch daran gedacht werden, daß die stark basischen Antibiotika direkt mit der Pantothensäure reagieren und es zur Bildung eines stabilen Streptomycin-Pantothenatkomplexes kommt. Hier

neurotoxische Erscheinungen, aber niemals Ohrschadigungen hervorrufen, stellt ein interessantes Phänomen dar das uns veranlaßte diese Substanzen mit in unsere Untersuchungen einzubeziehen

2 Die toxische Wirkung

Hinsichtlich der Ototoxizität der basischen Streptomycesantibiotika läßt sich folgende Reihenfolge aufstellen Die geringste toxische Wirkung besitzt offensichtlich Streptomycin danach folgen Dihydrostreptomycin Viomycin, Kanamycin Paromomycin *Framycetin schließlich Gentamycin und* als starkste toxische Verbindung dieser Gruppe das Neomycin

Bei der Streptomycinintoxikation wird grundsätzlich zwischen einer akuten *Vergiftung, der chronischen Intoxikation und organspezifischer* Wirkung unterschieden Die akute Toxizität der Aminoglykosidantibiotika soll hier nur am Rande betrachtet werden da sie mehr von theoretischem *Interesse*, für die *Praxis* wahrscheinlich aber bedeutungslos *ist* Akute Vergiftungen treten in den meisten Fällen nur bei intravenöser und intrathekaler Applikation oder bei intramuskulärer Injektion extrem hoher Dosen in Erscheinung Sie äußern sich zunächst in Erregungszustanden und Konvulsionen die in wenigen Minuten in eine allgemeine Lähmung der quergestreiften Muskulatur übergehen und schließlich zum Atemstillstand und Exitus letalis fuhren können Vom klinischen Standpunkt aus gesehen handelt es sich hier um das Symptomenbild einer Magnesiumvergiftung. Die meisten Magnesiumeffekte beruhen aber im Grunde genommen auf einer Verdrängung der Calciumionen (Hauschild, 1959) Auch der akuten Streptomycinintoxikation scheint ursächlich ein calcipriver Effekt zugrunde zu liegen, wofür z. B auch die Störung der Blutgerinnung spricht Jones (1959) gelang es, die neuromuskulären Symptome bei der Behandlung seiner Patienten mit Neomycin durch Calciumgaben günstig zu beeinflussen Nach Keller *et al* (1956) sollen die basischen Streptomycesantibiotika eine besondere Affinität zu den Calciumionen besitzen Tatsächlich konnte auch unter Streptomycin eine Verminderung des ionisierten Calciums bei unver*ändertem Gesamtcalciumgehalt nachgewiesen* werden

Durch Calciummangel kommt es, wie bereits Harvey und Macintosh (1930) feststellten, zu einer Storung der Erregungsübertragung und zu *Lähmungen die auf einem Aussetzen der Acetylcholinbildung am Nerven*ende beruhen sollen Schaefer (1940) führt die herabgesetzte Erregbarkeit auf eine erhöhte Permeabilität der Membranen infolge des Ca Mangels zurück *Auf die Bedeutung der Calciumionen für das Membranpotential* weist auch Brink hin Die Ca Verarmung hat einen neuromuskulären Block zur Folge der klinisch wie eine Curarerelaxation imponiert und darum auch als curareähnliche *Lähmung bezeichnet wird* Für einen solchen curareähnlichen Effekt der Aminoglykosidantibiotika sprechen auch die Befunde von Iwatsuki Ueda and Yamada (1960) sowie Füllmann und Reuter (1960) die am Hund *bzw an der Ratte unter* Streptomycin eine verstarkte Wirkung der repolarisationshemmenden Relaxantien d Tubocurarin und Cal

der Lage ist, die toxische Wirkung des Streptomycins weder am Hör noch am Gleichgewichtsorgan aufzuheben oder auch nur zu vermindern.

Mückter (1961) setzt sich in seiner Monographie eingehend mit den Möglichkeiten einer Entgiftung und den widersprechenden Befunden auseinander. In einer neueren Arbeit (Mückter 1966) wendet er sich gegen die vor kurzem wiederum von Kuschinsky (1966) geäußerte Ansicht, die Pantothensäure besäße keine entgiftende Wirkung. Mückter bemüht sich richtigzustellen, daß von seiner Seite niemals behauptet worden sei, die Pantothensäure verhindere ototoxische Schädigungen. Pantothensäure soll, so wird ausdrücklich betont, lediglich die Toleranz des Antibiotikums verbessern. Mückter verweist hier allein auf 59 teils experimentelle, teils klinische Arbeiten, die übereinstimmend für eine solche verbesserte Toleranz sprechen, während nur in 16 Arbeiten der Pantothensäureeffekt nicht reproduziert werden konnte. Die Befürworter der Pantothensäure können sich vor allem auf neuere Arbeiten berufen, die, verglichen mit älteren Untersuchungen aus den 50er Jahren, zu denen auch die Arbeiten von Kuschinsky, Löllmann und Pracht zu rechnen sind, unter verbesserten Versuchsbedingungen durchgeführt wurden. Besonders die elektrophysiologischen Untersuchungen Tybergheins und der Arbeitsgruppe Keidel, auf die bereits eingegangen wurde, werden hier hervorgehoben. Mit Hilfe histochemischer Methoden konnte auch Müsebeck unter Pantothensäure eine Herabsetzung der Streptomycintoxizität um etwa ein Drittel feststellen. Gegenteilige Berichte kommen, wie Müsebeck sehr richtig bemerkt, zum Teil dadurch zustande, daß die gewählte Dosis bereits über diesem Drittel der toxischen Grenzdosis liegt, so daß die Heraufsetzung der Verträglichkeitsgrenze durch die Pantothensäure nicht mehr zu erkennen ist. Besonders manchen experimentellen Arbeiten, so glaubt Müsebeck, in denen SM bewußt zur Erzeugung einer toxischen Reaktion weitaus höher dosiert wurde, liegt dieser Trugschluß einer angeblich fehlenden Schutzwirkung der Pantothenate zugrunde.

Nach Mückters Ansicht sind von den zahlreichen Substanzen, denen eine Herabsetzung der Toxizität bzw. eine toleranzverbessernde Wirkung zugeschrieben wird, nur das Calcium bei der akuten Vergiftung, im übrigen vor allem aber die Pantothensäure und wie sich in letzter Zeit zeigte, angeblich auch die Methansulfonatsalze der Streptomycesantibiotika sicher wirksam.

Dagegen haben alle anderen Vorschläge zur Toxizitätsminderung des Streptomycins keine praktische Bedeutung erlangt. So wurden neben der Pantothensäure auch noch andere Vitamine wie Ascorbinsäure, Nikotinsäure, p-Aminobenzoesäure, Vitamin A und Lactoflavin empfohlen.

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durch wird dem Organismus die für die Coenzym A-Synthese notwendige Pantothensäure entzogen Die toxischen Störungen die durch Streptomycin hervorgerufen werden, gleichen tatsächlich in mancher Hinsicht dem Symptomenbild eines Pantothensauremangels Die Entdeckung Kellers und seiner Mitarbeiter (1955 1956, 1956) daß durch Zusatz von Pantothensaure die Toxizität des SM herabgesetzt werden kann, wurde ebenfalls gut in diese Vorstellungen hineinpassen

Die Diskussion über die angeblich toxizitatsmindernde Eigenschaft der Pantothensäure ist bis heute noch in vollem Gang. Die Befunde Kellers und seiner Mitarbeiter denen man für die praktische Anwendung der Streptomycesantibiotika große Bedeutung beigemessen hat wurden in der Folgezeit von zahlreichen Untersuchern sowohl für die akute als auch für die chronische *Vergiftung nachgeprüft und bestätigt gefunden Vor allem* sollen die ototoxischen Erscheinungen durch Pantothensaure günstig beeinflußt werden (Keller Krüpe Sous und Mückter 1955 1956, 1956 Marquardt und Ziegler 1956 Ducrot Leau und Cosar 1956 Neumann und *Neubert 1958, und viele andere)*

Zu erwähnen sind vor allem die neueren Arbeiten der letzten Jahre von Tyberghein (1961 1962) Müsebeck (1964) sowie Hattig und Keidel (1965) die mit verbesserten Untersuchungsmethoden durchgeführt wurden *Die geringere Toxizität einige Pantothenatverbindungen konnte nicht* nur im Tierexperiment demonstriert werden sondern ließ sich auch beim Menschen nachweisen (Penman, Dickson und Miller 1957 Willemot Coossens, Pannier van der Calseyde 1959 Sievers, 1960 sowie Eckel und Altenburger *1960* u a)

Tyberghein verglich den Einfluß der verschiedenen Streptomycessubstanzen ihrer Sulfat Mono- Di und Tripantothenatsalze auf die Mikrophonpotentiale der Meerschweinchenschnecke Er fand nicht nur bei den Sulfat sondern auch bei den *Pantothenatverbindungen eine Abnahme der* Mikrophonpotentiale insbesondere in den hohen Frequenzen Nur die Streptomycindipantothenate und Kanamycinmonopantothenate riefen beim Meerschweinchen keine meßbaren Hörstorungen hervor Zu dem gleichen Ergebnis *kamen auch Hattig und Keidel* die elektrophysiologische Untersuchungen an der Katze durchführten Sie stellten fest daß von allen untersuchten Substanzen Kanamycinmonopantothenat das Hörorgan am wenigsten schadigt

Die Bedeutung der Pantothensaure *für die Entgiftung der Streptomyces* antibiotika blieb jedoch nicht ohne Widerspruch Osterberg und Mitarbeiter (1956/57) fanden lediglich eine geringere cochleotoxische Wirkung, aber keinen Einfluß auf die Vestibularisstorungen Zu vollständig negativen Ergebnissen *kamen dagegen Kimmerle und* Gosswald (1956) Hawkins, Wolcott und O'Shanny (1956/57) Child Davis, Sharpe und Tomich (1956/57) Clorig (1958) Brigham und Nielsen (1958) Des Anels (1959) Kuschinsky Lüllmann und Tracht (1960) sowie Wersäll und Hawkins (1962) Sie *stellen übereinstimmend* fest daß die Pantothensäure nicht in

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säure oder der Ascorbinsäure so auch hier mit dem sauren Heparin eine Verbindung eingehen können Aronson Meyer und Brock (1964) befaßten sich eingehend mit den Reaktionsmöglichkeiten des Streptomycins. Auf welche Weise das Kation SM mit den verschiedenen Verbindungen, wie Hyaluronsäure *Cephalin* Casein u a reagiert ob als Carbinolamin oder als Iminiumsalz, laßt sich danach noch nicht mit Sicherheit sagen

Die Tatsache daß die kationischen basischen Antibiotika eine besondere Affinität zu den sauren anionischen Substanzen besitzen ließ sich experimentell beweisen Durch Versuche in vitro konnte *gezeigt werden, daß sich* Heparin mit den Streptomyceesantibiotika verbindet wobei es zu einer echten Präzipitation kommt Wie Mora, Young und Shear (1959) feststellten, werden nicht nur die Basen Streptomycin und Neomycin, sondern auch andere basische Substanzen, wie die Polymyxine oder das Protamin durch anionische Polyglucosederivate gebunden und dadurch entgiftet Umgekehrt kann die Toxizität der basischen Antibiotika durch andere basische Makromoleküle wie *ACTH* gesteigert werden, indem diese in Konkurrenz mit den toxischen Antibiotika die sauren Substanzen des Organismus, die sonst *zur Entgiftung beitragen beschlagnahmen (Higginbotham und Dougherty* 1957)

Von der besonderen Affinität der basischen Streptomyceessubstanzen zu den sauren Mucopolysacchariden geht auch Müsebecks Theorie (1964) über die ototoxische Wirkungsweise *des Streptomycins aus. In einer früheren* Arbeit hatten bereits Müsebeck und Schätzle (1962) auf die Abnahme der sauren Mucopolysaccharide im Ligamentum spirale und im Limbus spiralis aufmerksam gemacht Als erstes *Zeichen* einer toxischen Schädigung beobachtete Müsebeck eine Veränderung in den proteingebundenen Sulfhydrylen *im Bereich der Stria vascularis des Innenohres.* Aus diesen histochemischen Befunden schließt Müsebeck daß die toxischen Antibiotika wahrscheinlich nicht gleichmäßig im Innenohr verteilt sind sondern hier bevorzugte Angriffspunkte und Retentionsorte besitzen Derartige bevorzugte Retentionsorte werden z B in dem mucopolysaccharidreichen Bindegewebe der Stria vascularis vermutet Von diesen Speicherungsorten aus soll nach Ansicht Müsebecks erst sekundär eine Schädigung der umgebenden Zellen insbesondere des Sinnesepithels, *erfolgen*

In jüngster Zeit sind allerdings Zweifel geäußert worden ob die mit histochemischen Methoden nachgewiesenen Sulfhydrylgruppen mit den sauren Mucopolysacchariden identisch sind Iurat (1965) konnte bei polarisationsmikroskopischen Untersuchungen weder in der Stria vascularis noch in der Membrana tectoria die bisher *als besonders mucopolysaccharidreich* angesehen wurde saure Mucopolysaccharide nachweisen Demnach müssen wahrscheinlich *bei den* Untersuchungen Müsebecks auch noch andere saure Substanzen in Betracht gezogen werden mit denen Streptomycin im Innenohr zu reagieren vermag Higginbotham sah bei den basischen Antibiotika vom Typ des Polymyxins und *Morikubo bei Kanamycin* eine Affinität zu den sauren Substraten des ZNS. Diese Reaktion kann

offenbar für alle Antibiotika der Aminoglykosidgruppe nicht nur im ZNS, sondern auch zu anderen sauren Verbindungen des Organismus angenommen werden.

Auf ähnliche Weise wie die sauren Mucopolysaccharide sollen auch Aminosäuren wie Leucin, Glycin oder Methionin mit den basischen Antibiotika reagieren und dadurch entgiftend wirken. Wahrscheinlich entstehen hier ebenfalls stabilere, komplexe Verbindungen zwischen dem Antibiotikum und der Aminosäure, die die Reaktionsfähigkeit der toxischen Substanz herabsetzen.

Cohen berichtete 1946, daß Streptomycin auch mit den Nukleinsäuren der Bakterienzelle reagiert. Diese Wirkung ist offenbar nicht nur auf die Bakterienzelle beschränkt, sondern scheint nach den Untersuchungen von Floberg, Hamberger und Hyden (1949) ebenso die Zellen des Organismus zu betreffen. Mit Hilfe der UV-Mikrospektrographie konnte man unter SM eine Verminderung des Nukleinsäuregehaltes der Nervenzellen, vor allem im Ganglion vestibulare nachweisen.

Die Tatsache, daß SM eine besondere Affinität zu den Nukleinsäuren nicht nur der Bakterien- sondern auch der Körperzellen besitzt, weist auf eine enge Beziehung zwischen dem toxischen und antibiotischen Wirkungsmechanismus hin. Wahrscheinlich beruhen beide auf dem gleichen Prinzip. Man muß sich darum fragen, ob eine Entgiftung des Streptomycins z. B. durch Kopplung an saure Substanzen wie Pantothensäure, Ascorbinsäure, Heparin, Aminosäuren oder Nukleinsäuren nicht gleichzeitig eine Herabsetzung der antibiotischen Wirksamkeit zur Folge hat.

Morikubo, Yamazaki, Takeuchi, Hikiji und Umezawa (1959) stellten bereits fest, daß durch die Bindung des Kanamycins an saure Phosphoproteine nicht nur die toxische Eigenschaft, sonder auch der antibiotische Effekt weitgehend aufgehoben werden.

Zu einem ähnlichen Ergebnis führte auch eine genauere Untersuchung der angeblich entgiftenden Wirkung *der Ascorbinsäure*, die von Prescott, Kaufmann, James und Stone (1959) und *nochmals 1962* von Krahl empfohlen wurde. Lagler und Sous (1965) *konnten* den Nachweis erbringen, daß die Ursache der geringeren Toxizität unter *dem Einfluß* der Ascorbinsäure auf einer *Herabsetzung des Streptomycinblutspiegels beruht*. Sie injizierten Ratten Kanamycin und zum Vergleich *einer* anderen Gruppe Kanamycin zusammen mit Na-Ascorbinat. *Es zeigte sich*, daß der Ka-Blutspiegel durch Ascorbinsäure um 50% *herabgesetzt wird*. Bei Meerschweinchen war dieser Effekt weniger stark *ausgeprägt*. Ascorbinsäure verminderte hier die Blutkonzentration nur *um 20%*. *In diesem* Fall stellt also die Toxizitätsminderung des Kanamycins keine *Entgiftung* im eigentlichen Sinne dar, sondern lediglich eine allgemeine Wirkungsminderung des Antibiotikums und zwar sowohl in toxischer als auch in antibiotischer Hinsicht. Der gleiche Effekt läßt sich aber genau so gut durch eine geringere Dosierung des Antibiotikums erzielen.

Auch die Antihistaminika erwiesen sich im Hinblick auf eine Entgif

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Die Tatsache, daß SM eine besondere Affinität zu den Nukleinsäuren nicht nur der Bakterien sondern auch der Körperzellen besitzt, weist auf eine enge Beziehung zwischen dem toxischen und antibiotischen Wirkungsmechanismus hin Wahrscheinlich beruhen beide auf dem gleichen Prinzip Man muß sich darum fragen, ob eine Entgiftung des Streptomycins z. B. durch Kopplung an saure Substanzen wie Pantothensäure, Ascorbinsäure Heparin, Aminosäuren oder Nukleinsäuren nicht gleichzeitig *eine* Herabsetzung der antibiotischen Wirksamkeit zur Folge hat.

Morikubo, Yamazaki, Takeuchi, Hikiji und Umezawa (1959) stellten bereits fest, daß durch die Bindung des Kanamycins an saure Phosphoproteine nicht nur die toxische Eigenschaft, sonder auch der antibiotische *Effekt* weitgehend aufgehoben werden

Zu einem ähnlichen Ergebnis führte auch eine genauere Untersuchung der angeblich entgiftenden Wirkung der Ascorbinsäure, *die von Prescott*, Kaufmann, James und Stone (1959) und nochmals 1962 von *Krahl empfohlen* wurde Lagler und Sous (1965) konnten den Nachweis erbringen, daß *die Ursache* der geringeren Toxizität unter dem Einfluß *der Ascorbinsäure* auf einer Herabsetzung des Streptomycinblutspiegels beruht Sie injizierten Ratten Kanamycin *und zum* Vergleich *einer* anderen Gruppe Kanamycin zusammen mit *Na-Ascorbinat* Es zeigte sich, daß der Ka Blutspiegel durch Ascorbinsäure um 50% herabgesetzt wird. Bei Meerschweinchen war dieser Effekt weniger stark ausgeprägt. Ascorbinsäure verminderte hier die Blutkonzentration nur um 20% *In diesem Fall* stellt also die Toxizitätsminderung des Kanamycins keine Entgiftung im eigentlichen Sinne dar sondern lediglich eine allgemeine Wirkungsminderung des Antibiotikums und zwar sowohl in toxischer als auch in antibiotischer Hinsicht. Der gleiche Effekt läßt *sich aber* genau so gut durch eine geringere Dosierung des Antibiotikums erzielen.

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säure oder der Ascorbinsäure so auch hier mit dem sauren Heparin eine Verbindung eingehen können Aronson Meyer und Brock (1964) befaßten sich eingehend mit den Reaktionsmöglichkeiten des Streptomycins. Auf welche Weise das Kation SM mit den verschiedenen Verbindungen wie Hyaluronsäure Cephalin Casein u a reagiert ob als Carbinolamin oder als Iminiumsalz, läßt sich danach noch nicht mit Sicherheit sagen

Die Tatsache daß die kationischen basischen Antibiotika eine besondere Affinität zu den sauren anionischen Substanzen besitzen ließ sich experimentell beweisen Durch Versuche in vitro konnte gezeigt werden daß sich Heparin mit den Streptomycesantibiotika verbindet wobei es zu einer echten Präzipitation kommt Wie Mora, Young und Shear (1959) feststellten werden nicht nur die Basen Streptomycin und Neomycin sondern auch andere basische Substanzen, wie die Polymyxine oder das Irotamin durch anionische Polyglucosederivate gebunden und dadurch entgiftet Umgekehrt kann die Toxizität der basischen Antibiotika durch andere basische Makromoleküle wie ACTH gesteigert werden, indem diese in Konkurrenz mit den toxischen Antibiotika die sauren Substanzen des Organismus, die sonst zur Entgiftung beitragen, beschlagnahmen (Higginbotham und Dougherty 1957)

Von der besonderen Affinität der basischen Streptomycessubstanzen zu den sauren Mucopolysacchariden geht auch Müsebecks Theorie (1964) über die ototoxische Wirkungsweise des Streptomycins aus. In einer früheren Arbeit hatten bereits Müsebeck und Schätzle (1962) auf die Abnahme der sauren Mucopolysaccharide im Ligamentum spirale und im Limbus spiralis aufmerksam gemacht Als erstes Zeichen einer toxischen Schädigung beobachtete Müsebeck eine Veränderung in den proteingebundenen Sulfhydrylen im Bereich der Stria vascularis des Innenohres. Aus diesen histochemischen Befunden schließt Müsebeck, daß die toxischen Antibiotika wahrscheinlich nicht gleichmäßig im Innenohr verteilt sind, sonder hier bevorzugte Angriffspunkte und Retentionsorte besitzen Derartige bevorzugte Retentionsorte werden z. B in dem mucopolysaccharidreichen Bindegewebe der Stria vascularis vermutet Von diesen Speicherungsorten aus soll nach Ansicht Müsebecks erst sekundär eine Schädigung der umgebenden Zellen insbesondere des Sinnesepithels, erfolgen

In jüngster Zeit sind allerdings Zweifel geäußert worden ob die mit histochemischen Methoden nachgewiesenen Sulfhydrylgruppen mit den sauren Mucopolysacchariden identisch sind Iurato (1965) konnte bei polarisationsmikroskopischen Untersuchungen weder in der Stria vascularis noch in der Membrana tectoria die bisher als besonders mucopolysaccharidreich angesehen wurde saure Mucopolysaccharide nachweisen Demnach müssen wahrscheinlich bei den Untersuchungen Müsebecks auch noch andere saure Substanzen in Betracht gezogen werden, mit denen Streptomycin im Innenohr zu reagieren vermag Higginbotham sah bei den basischen Antibiotika vom Typ des Polymyxins und Morikubo bei Kanamycin eine Affinität zu den sauren Substraten des ZNS. Diese Reaktion kann

offenbar für alle Antibiotika der Aminoglykosidgruppe nicht nur im ZNS, sondern auch zu anderen sauren Verbindungen des Organismus angenommen werden.

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tung des Streptomycins als unwirksam (Mückter 1961) Sie haben wahrscheinlich nur einen Einfluß auf die allergischen Nebenreaktionen, nicht aber auf die Ototoxizität des SM Allergische Reaktionen wurden vor allem früher bei ungereinigten Präparaten sehr häufig beobachtet und kommen heute nur noch selten vor Daneben muß aber auch berücksichtigt werden daß SM selbst ebenfalls die Eigenschaft eines Histaminliberators besitzt Radenbach und Amann (1959) konnten zeigen daß es unter SM und DSM zu einer Freisetzung endogenen Histamins aus den Mastzellen kommt Hierauf sind wahrscheinlich auch die gelegentlich zu beobachtenden Schmerzen an der Injektionsstelle sowie die juckenden Hautsensationen und Paraesthesien zurückzuführen Es wurde schon die Vermutung geäußert daß die allergischen Erscheinungen Vorläufer der Intoxikation darstellen Die Mehrzahl der Untersucher ist jedoch der Auffassung, daß zwischen der SM Allergie und der SM Vergiftung, insbesondere der Ototoxikose keine Beziehung besteht Andernfalls müßte mit den Antihistaminika eine Toxizitätsminderung zu erzielen sein was aber nach den Untersuchungen Laglers und seiner Mitarbeiter offensichtlich nicht der Fall ist

Zusammenfassend kann man sagen liegt den bisher betrachteten toxischen Reaktionen ein gemeinsames Prinzip zugrunde Danach reagieren die stark basischen Streptomycesantibiotika als Kationen mit sauren anionischen Substanzen des Organismus bzw auch der Bakterien Hierdurch entsteht so ist wenigstens die Ansicht der meisten Untersucher ein Mangel z. B an ionisiertem Calcium an Pantothensäure Coenzym A und anderen Enzymen an Aminosäuren oder Nukleinsäuren Der Entzug lebensnotwendiger Substanzen wird für die toxische aber auch für die antibiotische Wirkung ursächlich verantwortlich gemacht Es lag nahe durch Zusatz der genannten sauren Verbindungen zu versuchen die Toxizität herabzusetzen Dieses Verfahren hat jedoch den Nachteil daß hierdurch in den meisten Fällen auch die antibiotische Wirkung blockiert wird

Es erscheint jedoch zu einseitig, wollte man ausschließlich die basischen und kationischen Eigenschaften für die Toxizität der toxischen Streptomycesantibiotika verantwortlich machen Daneben müssen auch noch andere charakteristische Merkmale in Betracht gezogen werden Hauschild (1959) weist vor allem auf die Bedeutung der eigentümlichen Aminozuckergruppe hin die diese Antibiotika kennzeichnet Man stellt sich vor daß die N Methyl L-Glucosamingruppe des Streptomycins das physiologische D-Glucosamin der Tuberkelbazillen im Sinne einer competitive action verdrängt Ein solcher Mechanismus ist nicht nur für die antibiotische Wirkung anzunehmen sondern könnte darüber hinaus auch die toxischen Effekte an den Zellen des Organismus erklären

Die Bedeutung der Glucosamingruppe für die ototoxische Wirkung der Streptomycesantibiotika geht auch aus den Untersuchungen Owadas hervor Owada verglich die toxische Wirkung von Neomycin Kanamycin ihre Hydrolysationsprodukte und deren N Acetyl Derivate Es stellten sich dabei Unterschiede hinsichtlich der Allgemeintoxizität und des ototoxischen

Effektes heraus. Die LD_{50} war besonders niedrig bei Neomycin, etwas höher bei Kanamycin. Von den einzelnen Komponenten des Neomycin- und Kanamycinmoleküls erwies sich die 2-Deoxystreptamingruppe am toxischsten. Die allgemeine bzw. akute Toxizität kann demnach nicht auf eine einzelne Komponente des Neomycin- oder Kanamycinmoleküls zurückgeführt werden. Sie scheint vielmehr auf dem Gesamtmolekül zu beruhen.

Dagegen zeigte sich bei der Prüfung der ototoxischen Wirkung, daß 3-Glucosamin viel stärkere Hörschädigungen hervorruft als alle anderen untersuchten Substanzen. Es übertraf in dieser Hinsicht das 3-N-Acetyl-Glucosamin, Methyl-3-Glucosamin, 6-Glucosamin, aber auch Deoxystreptamin und sogar Kanamycin. Nur Neomycin war noch stärker ototoxisch als 3-Glucosamin. Owada schließt allerdings hieraus, daß auch die ototoxische Eigenschaft wahrscheinlich an das Gesamtmolekül der Streptomycesantibiotika gebunden ist. Zu der gleichen Ansicht kamen auch Aronson, Meyer und Brock (1964). Sie stellten ebenfalls fest, daß das SM-Molekül in seiner Gesamtheit ganz anders reagiert als seine Bausteine.

Neuere Vorstellungen und Erkenntnisse über den antibiotischen und toxischen Wirkungsmechanismus der Aminoglykosidantibiotika verdanken wir der Molekularbiologie. Während antibiotische und cytostatisch wirksame Substanzen, wie das Mitomycin, die DNS-Synthese oder das Actinomycin, die RNS-Synthese zu hemmen vermögen, haben die toxischen Streptomycesantibiotika im Gegensatz zu älteren Auffassungen offenbar auf die Nukleinsäuresynthese keinen Einfluß. Ihr Angriffspunkt ist vielmehr in der Proteinsynthese zu suchen, die durch Streptomycin unmittelbar und nicht erst über den Umweg einer Störung der DNS oder RNS blockiert wird.

Davies und Mitarbeiter (1964, 1965) und Gorini (1966) konnten im Experiment zeigen, daß sich Streptomycin an die eigentlichen Eiweißproduktionsstätten, die Ribosomen, anlagert. Nach Cox, White und Flaks (1964) wird Streptomycin an die 30-S-Untereinheiten der Ribosomen gebunden, an der Stelle, wo auch die Messenger-RNS sitzt. Streptomycin vermag die Ribosomen so zu verändern, daß sie die im genetischen Code chemisch verschlüsselten Anweisungen für die Proteinsynthese, die ihnen von der Messenger-RNS übermittelt werden, falsch interpretieren.

Verwendet man z. B. Polyuridylsäure, ein synthetisches Polynukleotid, als Messenger-RNS, so wird normalerweise nur Phenylalanin eingebaut. Unter dem Einfluß des Streptomycins wird der Phenylalanineinbau verringert. An Stelle von Phenylalanin werden jetzt andere Aminosäuren, vor allem Isoleucin und Serin, aber auch Tyrosin und Leucin eingebaut. Streptomycin führt also zur Neubildung nicht funktioneller Proteine mit abnormaler Aminosäurensequenz. Es entstehen sog. Nonsense-Polypeptide.

Auf ähnliche Weise lassen sich auch die Wirkungen anderer Antibiotika wie Chloramphenicol, Puromycin und Tetracyclin erklären. Sie greifen ebenfalls in die Proteinsynthese ein, jedoch an einer anderen Stelle als die Streptomycesantibiotika. So hemmt Chloramphenicol z. B. an der 50-S-

Untereinheit der Ribosomen die Ablösung der bereits fertigen Peptidketten vom Ribosom und behindert dadurch die Proteinsynthese

Eine 3 Möglichkeit einer Hemmung der Proteinsynthese konnte für Puromycein nachgewiesen werden Seine nahe chemisch strukturelle Verwandtschaft zur Amino-acryl Transfer RNS deutet schon auf den Wirkungsmechanismus hin Normalerweise wird im Verlauf der Proteinsynthese die Peptidkette von einem Transfer RNS-Molekül an das andere weitergereicht wobei sie jedesmal um eine weitere Aminosäure zunimmt In dem Augenblick aber wo sich die Peptidkette irrtümlich an das ähnlich aussehende Puromycin anhängt wird dieser Polymerisationsprozess unterbrochen und die unfertige Peptidkette löst sich vom Ribosom ab

Dellweg (1966) nimmt an, daß alle bekannten Effekte des Streptomycins, wie die Schädigung der Zytoplasmamembran Veränderungen der Zellwand und die Beeinflussung der oxydativen Phosphorylierung Folgeerscheinungen dieser spezifischen Hemmung der Proteinsynthese und einer hierdurch hervorgerufenen Änderung der Permeabilitätsschranke darstellen Nicht in allen Ribosomen vermag Streptomycin die Proteinsynthese in gleicher Weise momentan zu hemmen Die Wirkungen des Antibiotikums können sogar sehr unterschiedlich sein Das gilt sowohl für die Bakterien als auch für die Körperzellen Die Tatsache daß einige Zellen sensitiv die anderen resistent sind wird auf die unterschiedlichen Eigenschaften der jeweiligen Ribosomen zurückgeführt Auch durch Mutationen können Stämme entstehen, die resistent sind oder sogar solche die ein gewisses Streptomycinbedürfnis zeigen

Eine weitere interessante Theorie über die Wirkungsweise des Streptomycins entwickelten Hurwitz und Rosano (1965) Sie konnten im Experiment zeigen daß die tödliche Wirkung des Streptomycins und seine Fähigkeit in die Zelle einzudringen durch Chloramphenicol aufgehoben wird Dieses gelang jedoch nicht mehr wenn zuvor schon eine Streptomycinbehandlung mit niedrigen Dosen stattgefunden hatte Die Verfasser schließen hieraus auf eine durch Streptomycin induzierte Permease die es dem Antibiotikum erst ermöglichen soll *Permeabilitätsschranken zu überwinden* und in das Zellinnere zu gelangen Das würde in der heutigen Terminologie bedeuten daß unter Streptomycin zunächst eine de novo-Synthese einer spezifischen Messenger RNS, auch Transcription genannt erfolgen muß, die in den Ribosomen die Synthese eines neuen spezifischen Proteins, einer *Permease eine sog Translation,* veranlaßt Durch Chloramphenicol soll die Synthese der spezifischen Permease in den Ribosomen gehemmt und dadurch die Streptomycineinwirkung aufgehoben werden Der entgiftende Effekt des Chloramphenicols wird daher unwirksam wenn schon vorher Streptomycin gegeben wurde und die Synthese der Permease bereits erfolgt ist

In jüngster Zeit berichteten Holz, Stange und Terravama über aufsehenerregende Erfolge mit Ozothin das die Giftwirkung des SM und aller anderen *Oligosaccharidantibiotika aufheben* soll Ozothin ist die Waren

bezeichnung für ein Kombinationspräparat aus Oxydationsprodukten des Oleum Terebinthinae und Terpinum hydratum, das klinisch als Expectorans Anwendung findet, aber auch als Lösungsmittel für Antibiotika empfohlen wird. Bis heute fehlt es an fundierten Vorstellungen über den Wirkungsmechanismus des Ozothins, insbesondere auch hinsichtlich der entgiftenden Eigenschaft.

Die große Zahl der zur Entgiftung empfohlenen Substanzen, von denen die meisten einer genaueren Nachprüfung nicht standhielten, beweist, mit welcher Vorsicht eine Entgiftung zu bewerten ist. Die wichtigsten Substanzen, die z. Zt. im Mittelpunkt der Diskussion stehen, wie das Ozothin und die verschiedenen Pantothenatsalze der Aminoglykosidantibiotika wurden mit in unsere Versuchsreihe aufgenommen und im Rahmen unsere Fragestellung auf ihre angeblich entgiftende Wirkung hin untersucht

C NEUE ASPEKTE UND EXPERIMENTELLE UNTERSUCHUNGEN

I Die Organspezifität der Streptomycinvergiftung und ihre Abgrenzung gegenüber unspezifischen Ototoxikosen

Die spezifischen Ototoxikosen stellen eine Sonderform der Innenohrintoxikation dar Daß der N statoacusticus häufiger als andere Hirnnerven durch Gifte verschiedenster Art geschädigt wird, stellte Taylor bereits im Jahre 1937 fest Von den zahlreichen Substanzen, die eine Innenohrschädigung hervorrufen können, seien hier nur das Arsenik, Oleum chenopodii, Jodkalium, Chloroform Jodoform Alkaloide verschiedene Gase wie Kohlenmonoxyd Chlor Phosgen, Cyan Acetylen Schwefelwasserstoff u a Schwermetalle (Ag, Hg und Pb) oder Nitrobenzol, Anilin und Phosphor und, wie vielfach angenommen wird auch Alkohol und Nikotin erwähnt

Größere praktische Bedeutung erlangten die Hörverluste nach Chinin vor allem bei der Bekämpfung der Malaria die eine langer dauernde und höher dosierte Behandlung erforderte Aber selbst unter so harmlos erscheinenden *Medikamenten wie Aspirin und anderen Salicylsäurepräparaten* stellten sich Hörschädigungen ein die allerdings i G zum Chinin weniger stark ausgeprägt und vor allem stets reversibel sind (Wittmaack 1903 Pohlmann und Kranz, 1922 Covell 1936 Falbe Hansen 1941 Jager und Alway 1946 Graham und Parker 1948 Waltener 1956 McCabe und Dey 1965 Myers und Bernstein, 1965)

Covell verglich an Kaninchen, Meerschweinchen und Mausen die Veränderungen die durch Chinin und Salicylate hervorgerufen werden Die Substanzen wiesen ein unterschiedliches Schädigungsbild auf Salicylsäure scheint gegenüber Chinin bevorzugt die Zellen des Ganglion cochleae zu treffen

Auch der klinische Verlauf der Innenohrintoxikation ist bei beiden Substanzen verschieden Horschaden durch Chinin sind in der Regel nicht mehr rückbildungsfähig Sie konnen sogar nach Absetzen des Medikamentes noch weiter fortschreiten Dagegen bilden sich die Ohrgeräusche Schwindelerscheinungen und die Schwerhörigkeit nach Aspirin die selten 40 dB überschreitet innerhalb von 72 Stunden nach Absetzen des Präparates vollständig zurück Die Salicylototoxikose soll nach Myers und Bernstein so risikolos sein daß sie ohne Bedenken zur Erzeugung experimenteller Hörstörungen beim Menschen angewandt werden kann

Kapur (1965) teilte allerdings einen Fall mit bei dem im Rahmen eines fieberhaften Infektes bereits nach 3 Apsirintabletten eine Taubheit eintrat Er vermutet daß hier eine besondere Überempfindlichkeit vorgelegen hat

Auf eine Überempfindlichkeit gegenüber Aspirin wies Taylor schon im Jahre 1937 hin. Eine permanente Ertaubung durch Aspirin stellt nach seiner Meinung eine Ausnahme dar und ist nur bei einer sog. Idiosynkrasie gegen dieses Medikament zu erwarten

Diese vereinzelten Beobachtungen widersprechen den klinischen und experimentellen Befunden Myers, Bernsteins und der anderen Autoren. Die Entscheidung, ob Salicylate ursächlich für eine Hörstörung in Betracht kommen, ist in einzelnen Beobachtungsfällen sehr schwierig und kann höchstens mit einer gewissen Wahrscheinlichkeit getroffen werden. Es ist stets dabei zu bedenken, daß plötzliche Ertaubungen unter der Bezeichnung „akuter Hörsturz" oder „sudden deafness" ein bekanntes und nicht einmal seltenes Krankheitsbild darstellen, das in den meisten Fällen ohne jede erkennbare Ursache auftritt. Im allgemeinen werden hierfür Durchblutungsstörungen verschiedenster Art oder Virusinfekte angeschuldigt (Neveling, 1963) In Anbetracht der außerordentlich weiten Verbreitung der Salicylatanwendung könnte es sich deshalb um zufällig zeitlich zusammenfallende Ereignisse handeln, die in keiner ursächlichen Beziehung zueinander stehen. Diese Möglichkeit ist auch bei dem von Kapur mitgeteilten Fall zu berücksichtigen. Allein durch den fieberhaften Infekt könnte hier die Schwerhörigkeit hervorgerufen worden sein.

Erst recht ist die vor kurzem von Jarvis (1966) beschriebene einseitige Ertaubung nach Aspirin mit Zurückhaltung zu beurteilen, nicht nur weil toxische Schädigungen in der Regel beide Ohren treffen Vor allem ist hier auffällig, daß ausgerechnet die Seite ertaubte auf der die ausgedehnte phlegmonöse Entzündung der einen Gesichtshälfte bestand, derentwegen letztlich die Aspirinbehandlung erfolgte. Auch hier spricht vieles dafür daß die Primärerkrankung die Ursache der Hörstörung ist.

Von diesen wenigen und umstrittenen Ausnahmen abgesehen, kann für alle oben aufgeführten ototoxischen Substanzen das gleiche Wirkungsprinzip angenommen werden. Ihre toxische Wirkung ist aus folgenden Gründen als unspezifisch zu bezeichnen

1 weil eine Schädigung nur bei extrem hoher Dosierung auftritt, also bereit Ausdruck einer Überdosierung ist, und
2. weil sie nicht ausschließlich auf das Innenohr oder einige wenige Organe beschränkt und damit nicht organspezifisch ist.

Die Innenohrschädigung stellt hier lediglich ein Symptom eines komplexen Vergiftungsbildes unter vielen anderen dar Die Schwerhörigkeit steht allerdings deswegen häufig im Vordergrund und erregt besondere Aufmerksamkeit, weil sie meistens irreparabel ist und als ein besonders auffälliges Symptom bestehen bleibt, während die anderen toxischen Erscheinungen längst abgeklungen sind.

Im Gegensatz hierzu zeichnen sich die Streptomyceantibiotika der Oligosaccharidgruppe dadurch aus, daß sie schon in sog. therapeutischen Dosen zu Schädigungen führen, die bemerkenswerterweise ausschließlich das

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Auch der klinische Verlauf der Innenohrintoxikation ist bei beiden Substanzen verschieden Hörschäden durch Chinin sind in der Regel nicht mehr rückbildungsfähig. Sie können sogar nach Absetzen des Medikamentes noch weiter fortschreiten Dagegen bilden sich die Ohrgeräusche Schwindelerscheinungen und die Schwerhörigkeit nach Aspirin, die selten 40 dB überschreitet, innerhalb von 72 Stunden nach Absetzen des Präparates vollständig zurück Die Salicylototoxikose soll nach Myers und Bernstein so risikolos sein daß sie ohne Bedenken zur Erzeugung experimenteller Hörstörungen beim Menschen angewandt werden kann

Kapur (1965) teilte allerdings einen Fall mit bei dem im Rahmen eines fieberhaften Infektes bereits nach 3 Aspirintabletten eine Taubheit eintrat Er vermutet daß hier eine besondere Überempfindlichkeit vorgelegen hat

Auf eine Überempfindlichkeit gegenüber Aspirin wies Taylor schon im Jahre 1937 hin. Eine permanente Ertaubung durch Aspirin stellt nach seiner Meinung eine Ausnahme dar und ist nur bei einer sog. Idiosynkrasie gegen dieses Medikament zu erwarten.

Diese vereinzelten Beobachtungen widersprechen den klinischen und experimentellen Befunden Myers, Bernsteins und der anderen Autoren. Die Entscheidung, ob Salicylate ursächlich für eine Hörstörung in Betracht kommen, ist in einzelnen Beobachtungsfällen sehr schwierig und kann höchstens mit einer gewissen Wahrscheinlichkeit getroffen werden. Es ist stets dabei zu bedenken, daß plötzliche Ertaubungen unter der Bezeichnung „akuter Hörsturz" oder „sudden deafness" ein bekanntes und nicht einmal seltenes Krankheitsbild darstellen, das in den meisten Fällen ohne jede erkennbare Ursache auftritt. Im allgemeinen werden hierfür Durchblutungsstörungen verschiedenster Art oder Virusinfekte angeschuldigt (Neveling, 1963). In Anbetracht der außerordentlich weiten Verbreitung der Salicylatanwendung könnte es sich deshalb um zufällig zeitlich zusammenfallende Ereignisse handeln, die in keiner ursächlichen Beziehung zueinander stehen. Diese Möglichkeit ist auch bei dem von Kapur mitgeteilten Fall zu berücksichtigen. Allein durch den fieberhaften Infekt könnte hier die Schwerhörigkeit hervorgerufen worden sein.

Erst recht ist die vor kurzem von Jarvis (1966) beschriebene einseitige Ertaubung nach Aspirin mit Zurückhaltung zu beurteilen, nicht nur weil toxische Schädigungen in der Regel beide Ohren treffen. Vor allem ist hier auffällig, daß ausgerechnet die Seite ertaubte, auf der die ausgedehnte phlegmonöse Entzündung der einen Gesichtshälfte bestand, derentwegen letztlich die Aspirinbehandlung erfolgte. Auch hier spricht vieles dafür, daß die Primärerkrankung die Ursache der Hörstörung ist.

Von diesen wenigen und umstrittenen Ausnahmen abgesehen, kann für alle oben aufgeführten ototoxischen Substanzen das gleiche Wirkungsprinzip angenommen werden. Ihre toxische Wirkung ist aus folgenden Gründen als unspezifisch zu bezeichnen:

1. weil eine Schädigung nur bei extrem hoher Dosierung auftritt, also bereits Ausdruck einer Überdosierung ist, und
2. weil sie nicht ausschließlich auf das Innenohr oder einige wenige Organe beschränkt und damit nicht organspezifisch ist.

Die Innenohrschädigung stellt hier lediglich ein Symptom eines komplexen Vergiftungsbildes unter vielen anderen dar. Die Schwerhörigkeit steht allerdings deswegen häufig im Vordergrund und erregt besondere Aufmerksamkeit, weil sie meistens irreparabel ist und als ein besonders auffälliges Symptom bestehen bleibt, während die anderen toxischen Erscheinungen längst abgeklungen sind.

Im Gegensatz hierzu zeichnen sich die Streptomycesantibiotika der Oligosaccharidgruppe dadurch aus, daß sie schon in sog. therapeutischen Dosen zu Schädigungen führen, die bemerkenswerterweise ausschließlich das

C. NEUE ASPEKTE UND EXPERIMENTELLE UNTERSUCHUNGEN

I. Die Organspezifität der Streptomycinvergiftung und ihre Abgrenzung gegenüber unspezifischen Ototoxikosen

Die spezifischen Ototoxikosen stellen eine Sonderform der Innenohrintoxikation dar. Daß der N. statoacusticus häufiger als andere Hirnnerven durch Gifte verschiedenster Art geschädigt wird, stellte Taylor bereits im Jahre 1937 fest. Von den zahlreichen Substanzen, die eine Innenohrschädigung hervorrufen können, seien hier nur das Arsenik, Oleum chenopodii, Jodkalium, Chloroform, Jodoform, Alkaloide, verschiedene Gase wie Kohlenmonoxyd, Chlor, Phosgen, Cyan, Acetylen, Schwefelwasserstoff u. a., Schwermetalle (Ag, Hg und Pb) oder Nitrobenzol, Anilin und Phosphor und, wie vielfach angenommen wird, auch Alkohol und Nikotin erwähnt.

Größere praktische Bedeutung erlangten die Hörverluste nach Chinin, vor allem bei der Bekämpfung der Malaria, die eine langer dauernde und höher dosierte Behandlung erforderte. Aber selbst unter so harmlos erscheinenden Medikamenten wie Aspirin und anderen Salicylsäurepräparaten stellten sich Hörschädigungen ein, die allerdings i. G. zum Chinin weniger stark ausgeprägt und vor allem stets reversibel sind (Wittmaack, 1903; Pohlmann und Kranz, 1922; Covell, 1936; Falbe-Hansen, 1941; Jager und Alway, 1946; Graham und Parker, 1948; Waltener, 1956; McCabe und Dey, 1965; Myers und Bernstein, 1965).

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(Buggs, Pilling, Bornstein und Hirsfeld, 1946 Marshall 1948 Levin, Carr und Hellman, 1946 Rake, Pansy Jambor und Donovick, 1948 Cronk und Naumann, 1959)

Ihre charakteristischen Permeationseigenschaften erklären, warum sie nicht gleichmäßig im Organismus verteilt sind, sondern in den einzelnen Organen in sehr unterschiedlichen Konzentrationen vorkommen.

Aufschluß über die Verteilung und das Konzentrationszeitverhalten der basischen Streptomycesantibiotika geben die Untersuchungen Andrés, die mit tritiummarkiertem DSM durchgeführt wurden Nach intravenöser Injektion dieser Substanz stellte sich zunächst für eine kurze Zeit ein hoher Blutspiegel ein. Wenig später ließen sich vor allem in der Lunge, im Bindegewebe im Knorpel und in der Niere hohe DSM Konzentrationen nachweisen, die etwa die Höhe des Blutspeigels erreichten. Nur das Gehirn fiel durch einen besonders niedrigen DSM-Gehalt auf der lediglich 16% der Blutkonzentration ausmachte. Der DSM-Gehalt des Innenohres wurde bei der von André, wahrscheinlich wegen der technischen Schwierigkeiten, nicht untersucht. Bereits nach 320 Minuten post inject. war DSM, wie Torsten André zeigen konnte, aus dem Blut und aus den meisten Organen wieder weitgehend eliminiert. Aber im Knorpelgewebe und in den Ausscheidungsorganen, der Niere, der Leber und den Gallenwegen sowie im Darm, fanden sich zu diesem Zeitpunkt immer noch mittlere DSM Konzentrationen.

Die Aminoglykosidantibiotika werden praktisch unverändert zum überwiegenden Teil durch die Nieren aber auch über die Leber und *Galle via* Darm ausgeschieden. Wie Clearanceuntersuchungen *zeigten, erfolgt* die renale Ausscheidung ausschließlich durch *glomeruläre Filtration* und nicht durch aktive Sekretionsleistungen der *Tubuluszellen (Edison*, Jelinek und *Boxer 1949)* Wie oben bereits erwähnt wurde findet auch praktisch keine tubuläre Rückresorption dieser Substanzen statt

Stoemmler und Dudkowiak (1961) konnten allerdings eine Speicherung *der toxischen* Streptomycesantibiotika in den Tubulusepithelien feststellen. Die *Anreicherung in* den Tubuluszellen war bei *den einzelnen* Antibiotika unterschiedlich stark ausgeprägt Interessanterweise lagerten sich die stärksten oto- und nephrotoxischen Substanzen auch am *meisten* in den *Tubuli ab* So fand man hier vor allem hohe *Konzentrationen* von Neomycin, auch Kanamycin, weniger dagegen DSM und am *wenigsten* SM

Man muß sich fragen, worauf diese unterschiedliche Anreicherung zurückzuführen ist Ist es das *charakteristische* Permeationsverhalten, insbesondere die schlechte Resorbierbarkeit *dieser Substanzen*, die zu den Ablagerungen und schließlich zur toxischen Schädigung führt Oder sind die Ablagerungen nicht die Ursache sondern nur eine Folge der toxischen Wirkung? Die Vermutung liegt zwar nahe daß durch die Speicherung der toxischen Antibiotika in den Tubuluszellen eine *Störung* und Schädigung hervorgerufen wird. Umgekehrt könnte man sich aber auch vorstellen, daß die Streptomycesantibiotika erst sekundär in den *toxisch geschädigten* Zel

Innenohr und die Niere betreffen. Nur ihre toxische Wirkung kann deshalb als organspezifisch bezeichnet werden. Im folgenden soll versucht werden, die Ursache der Organspezifität zu erklären.

II. Die Permeationseigenschaften und die Verteilung der Aminoglykosidantibiotika im Organismus

Bei den bisher betrachteten toxikologischen Untersuchungen standen vor allem zwei Eigenschaften: der stark basische Charakter und die Zuckerkomponente des Streptomycinmoleküls im *Vordergrund*. *Darüberhinaus* zeichnen sich die toxischen Streptomyceesantibiotika gegenüber den anderen antibiotischen Substanzen noch durch ein weiteres gemeinsames Merkmal aus, nämlich ihr besonders schlechtes Permeationsvermögen. Diesem eigentümlichen Verhalten der Oligosaccharidantibiotika wurde bis heute keine Beachtung geschenkt. Für die Entstehung der organspezifischen Vergiftungen scheint ihm jedoch eine besondere Bedeutung zuzukommen.

Es ist auffällig, daß alle toxischen Antibiotika sowohl die der Aminoglykosidgruppe als auch die Polymyxine mit Polypeptidstruktur nicht resorbiert werden können. Sie finden sich überwiegend im extrazellulären Raum. Nach *Robson und Sullivan* (1963) vermag *Streptomycin* und das gleiche muß auch für die verwandten Substanzen dieser Gruppe angenommen werden, nur sehr schlecht in die Zelle einzudringen. So ist auch zu verstehen, warum diese Stoffe von den Zellen nicht aktiv sezerniert werden können. Im Blut fand Torsten André (1956) tritiummarkiertes DSM nur im Plasma nicht aber in den zellulären Elementen, den roten und weißen Blutkörperchen. Auch die Epithelien der Darmmucosa und der Nierentubuli sind offenbar nicht in der Lage, diese unphysiologischen Oligosaccharide aktiv aufzunehmen, zu resorbieren. Für den Transport der basischen Antibiotika innerhalb des Organismus kommen daher praktisch *ausschließlich passive* Vorgänge wie *Diffusion oder Filtration* in Betracht. Das Verhalten der Oligosaccharidantibiotika erinnert in dieser Hinsicht sehr an Substanzen wie Inulin oder Mannitol, die auf Grund dieser besonderen Eigenschaften zur Bestimmung des Extrazellularraumes oder bei Clearanceuntersuchungen zur Feststellung der Filtrationsgröße Anwendung finden. Auf Inulin soll deswegen an anderer Stelle noch näher eingegangen werden.

Die Möglichkeit, auf passivem Wege in die *Zelle* zu *diffundieren*, *scheint* zumindest für das Streptomycinmolekül nur eine untergeordnete und im allgemeinen zu vernachlässigende Rolle zu spielen. Nur bei besonders hohen Antibiotikakonzentrationen, wie sie z. B. in den Nierentubuli anzutreffen sind, scheinen, durch das steile Konzentrationsgefälle begünstigt, größere Mengen der toxischen Substanzen in die oberflächlichen Epithelschichten eindringen zu können.

Alle Antibiotika der Aminoglykosidgruppe *verhalten sich hinsichtlich* ihrer Resorption, Verteilung und Ausscheidung grundsätzlich ähnlich.

spezifisch hohen Antibiotikagehalt der Innenohrflüssigkeiten zurückzuführen ist.

Höhere Konzentrationen der Aminoglykosidantibiotika finden sich, wie bereits erwähnt wurde, nicht nur in der Niere sondern auch im Darm. Der Resorptionsprozeß des Darmes weist bemerkenswerte Analogien zu den Vorgängen in den Nierentubuli auf (Stupp, 1960 Rummel und Stupp, 1960 und 1962) Der Darm vermag ebenfalls die toxischen Antibiotika nicht zu resorbieren. Deshalb eignen sich die Streptomycessubstanzen auch besonders gut zur präoperativen Darmsterilisation. Bei den hier angewandten extrem hohen Dosen konnte allerdings beobachtet werden, daß unter diesen Bedingungen etwa 3% vom Darm aufgenommen werden und in den Organismus gelangen. So ist es zu erklären, daß auch bei enteraler Applikation u. U Intoxikationserscheinungen vorkommen können.

Ähnlich wie bei der Harnkonzentration in den Nierentubuli erfahren die toxischen Antibiotika im Verlaufe der enteralen Resorption eine Anreicherung. Während der größte Teil des Darminhaltes der Resorption unterliegt, bleiben die nicht resorbierbaren Antibiotika im Darm zurück und erreichen hier höhere Konzentrationen.

Nicht nur in funktioneller Hinsicht, sondern auch im elektronenmikroskopischen Bild, lassen sich übereinstimmende Merkmale zwischen den Epithelien des Darmes und des Nierentubulus erkennen. Enge morphologische und funktionelle Beziehungen bestehen nach Rauch (1961) aber auch zwischen den Nierenepithelien und dem Epithel der Stria vascularis des Innenohres, einer Epithelschicht, die durch eine besonders starke Vascularisation und intensiven Stoffwechsel auffällt. Sie kleidet die laterale Wand des Endolymphraumes aus und wird als Resorptionsort für die Innenohrflüssigkeiten angesehen (Abb. 1)

Dem Darm kommt hier insofern eine Bedeutung zu, da er für unsere Untersuchungen zur Klärung des Schädigungsweges die weitaus günstig

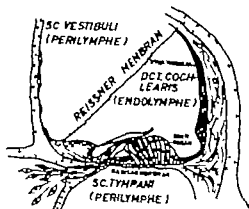


Abb 1 Anatomie des Innenohres.

len abgelagert werden und das Ausmaß dieser Ablagerung nur Ausdruck der Stärke der Schädigung ist

III Untersuchungen zur Frage des Intoxikationsweges

Auf welchem Wege Kanamycin in die Tubuluszellen gelangt ob durch Rückresorption aus dem Tubuluslumen oder aus entgegengesetzter Richtung durch direkte Aufnahme aus dem Blutkreislauf wagte Mückter (1961) nicht zu entscheiden Die Streptomycesantibiotika erreichen da sie nicht rückresorbiert werden können *in den Nierentubuli im Gefolge* der Harnkonzentrierung die weitaus hochsten Konzentrationen die überhaupt im *Organismus feststellbar sind* Messungen des Kanamycingehaltes im Harn ergaben Werte, die den höchsten Blutspiegel noch um mehr als das 150-fache übertreffen (Stupp *et al.*, 1965) In Anbetracht des viel niedrigeren Blutspiegels erscheint eine vom Blut ausgehende Schädigung wenig wahrscheinlich Wäre dies der Fall so müßte man erwarten, da die Blutkonzentration annähernd überall gleich hoch ist daß andere Zellen *genauso von der Giftwirkung in Mitleidenschaft* gezogen werden Es wäre dann nicht einzusehen warum ausgerechnet die Tubulusepithelien geschädigt werden. Die Tatsache daß nur die oberflächlichen Epithelschichten betroffen sind scheint für die Annahme zu sprechen, daß die Schädigung vom Tubuluslumen aus erfolgt und wahrscheinlich auf die extrem hohe Konzentration im Primärharn zurückzuführen ist

Die Frage des Schädigungsweges ist für das Verständnis des toxischen Wirkungsmechanismus von grundlegender Bedeutung. Erfolgt nämlich die Schädigung der Tubuli vom Blut aus, so würde das bedeuten daß die Tubulusepithelien im Vergleich mit anderen Zellen, die der gleichen Blutkonzentration ausgesetzt sind besonders empfindlich sind. Für den Fall aber daß die toxischen Substanzen unmittelbar vom Tubuluslumen aus auf die Tubulusepithelien einwirken, müßte die Schadigung als Folge der hohen Antibiotikakonzentration *im Harn aufgefaßt* werden Das hieße aber mit anderen Worten, die Intoxikation beruht nicht auf einer organspezifischen Sensibilität der Niere, sondern in erster Linie auf der spezifisch hohen Antibiotikakonzentration

Der Weg, auf dem die toxischen Antibiotika den Schädigungsort erreichen verdient deswegen eine eingehendere Betrachtung, weil für das Innenohr sehr ähnliche Verhaltnisse anzunehmen sind Auch hier stehen wir vor der gleichen Frage erfolgt die Schadigung von der Blutseite her d h., zeichnet sich das Innenohr durch eine spezifische Empfindlichkeit aus, wie heute noch allgemein angenommen wird oder findet sie von den Innenohrraumen und den Innenohrflüssigkeiten aus statt Im letzteren Fall müßte daran gedacht werden *ob nicht im Innenohr ähnlich* wie in den Nierentubuli besonders hohe Antibiotikakonzentrationen vorkommen Hiermit würde auch die Frage *entschieden, ob die sog. spezifische* Ototoxikose auf einer spezifischen Sensibilität des Innenohres *beruht oder ob sie auf einem*

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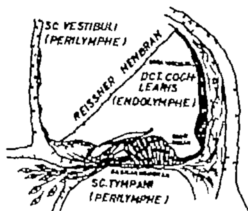


Abb. 1. Anatomie des Innenohres.

sten Versuchsbedingungen bietet Er diente gleichsam als Modell zum Studium des Intoxikationsmechanismus und insbesondere des Schädigungsweges von dem man annehmen darf daß er wahrscheinlich in den Nierentubuli und Innenohrräumen ähnlich verläuft dessen Untersuchung hier aber aus verständlichen methodischen Gründen viel schwieriger ist Ziel dieser Untersuchungen war es vor allem festzustellen ob Kanamycin trotz seiner bekannten schlechten Resorbierbarkeit in der Lage ist vom Darmlumen aus, also unter Umgehung des Blutweges, auf die Darmepithelien einzuwirken und diese unter Umständen zu schädigen Zu diesem Zweck wurden Dünndarmabschnitte am lebenden narkotisierten Meerschweinchen mit Kanamycinsulfatlösungen und in benachbarten Abschnitten zum Vergleich mit Ringerlösung gefüllt und dann verschlossen

Methode

Als Versuchstiere dienten Meerschweinchen mit einem durchschnittlichen Gewicht von 250 g. Die Tiere erhielten als Basisnarkotikum 10 mg Urethan/kg intraperitoneal und zusätzlich eine Ätherinhalationsnarkose Nach Eröffnung des Abdomens wurden 2 gleich lange Jejunumabschnitte freigelegt und unter Erhaltung der Durchblutung die Darmlumen eröffnet Zunächst wurde der Darm zur Reinigung mit Ringerlösung durchspült und anschließend in einen Darmabschnitt eine isotone 15%ige Kanamycinsulfatlösung mit einem PH von 6 8 und in den anderen ein gleich großes Volumen Ringerlösung gefüllt Danach wurde das Darmlumen durch eine Unterbindung abgeschlossen die Darmstücke wieder in die Bauchhöhle zurückverlagert und die Bauchdecke verschlossen Der Darminhalt wurde nach 14 Stunden Versuchsdauer gewogen und das Gewebe zur histologischen Untersuchung in Formalinlösung fixiert eingebettet und nach Heidenhain mit Hämatoxylin Eosin gefärbt

Ergebnisse

In dem Darmabschnitt der Kanamycin enthielt fiel verglichen mit dem benachbarten Kontrolldarmstück zunächst eine ausgeprägte Hyperämie auf Der Darm erschien hochrot bis leicht bläulich verfärbt Die gleiche Beobachtung machte Müsebeck (1962) auch am Innenohr nach SM Intoxikationen

Im weiteren Verlauf zeigte es sich daß die Ringerlösung wesentlich schneller resorbiert wird Der Resorptionsprozeß war unter Kanamycin offensichtlich gehemmt Am Ende des Versuches war der Kanamycin enthaltende Darm fast genauso voll wie zu Beginn während der Kontrolldarm praktisch leer war Auf die Bestimmung des Kanamycingehaltes wurde bei diesen Untersuchungen die lediglich orientierenden Charakter haben sollen verzichtet zumal die schlechte Resorbierbarkeit des Kanamycins allgemein bekannt ist

Uns interessieren vor allem die histologischen Veränderungen an den

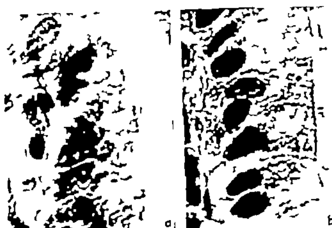


Abb. 2. ( ) Darmepithelien nter Kanamycin, (b) Kontrolldarm (Ringerlösung)

Darmepithelien, wie sie auf Abb 2 a und Abb 3 a und zum Vergleich in den Kontrolldarmabschnitten Abb. 2 b und Abb. 3 b zu erkennen sind.

Hier zeigt sich ein sehr ähnliches Schädigungsbild, wie es bereits von den Tubuluszellen und vom Innenohr bekannt ist und übereinstimmend von zahlreichen Autoren beschrieben wurde Die Mucosazellen waren unter Kanamycin deutlich vergrößert, aufgetrieben und ihre Zellgrenzen nicht mehr zu erkennen. In den Zellen fanden sich große Vacuolen. Am auffälligsten war die Vergroßerung und Schwellung der Zellkerne Sie fielen außerdem durch eine intensivere Färbung und eine unregelmäßige Form auf Ein Nucleolus ließ sich nicht mehr feststellen. Demgegenüber konnten am Kontrolldarm keine pathologischen Veränderungen festgestellt werden Die Zellkerne waren hier viel kleiner rundlich bis oval. Sie besaßen in ihrer

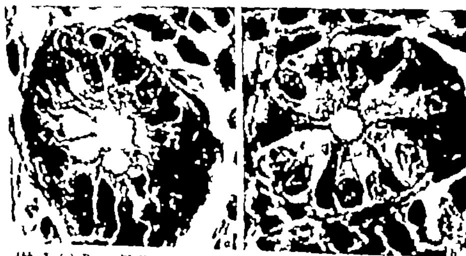


Abb 3. ( ) Darmepithelien nter Kanamyci mit großen, intrazell ären V cuolen. (b) Kontrolldarm (Ringerlösung)

sten Versuchsbedingungen bietet. Er diente gleichsam als Modell zum Studium des Intoxikationsmechanismus und insbesondere des Schädigungsweges, von dem man annehmen darf, daß er wahrscheinlich in den Nierentubuli und Innenohrräumen ähnlich verläuft, dessen Untersuchung hier aber aus verständlichen methodischen Gründen viel schwieriger ist. Ziel dieser Untersuchungen war es vor allem festzustellen, ob Kanamycin trotz seiner bekannten schlechten Resorbierbarkeit in der Lage ist, vom Darmlumen aus, also unter Umgehung des Blutweges, auf die Darmepithelien einzuwirken und diese unter Umständen zu schädigen. Zu diesem Zweck wurden Dünndarmabschnitte am lebenden narkotisierten Meerschweinchen mit Kanamycinsulfatlösungen und in benachbarten Abschnitten zum Vergleich mit Ringerlösung gefüllt und dann verschlossen.

Methode

Als Versuchstiere dienten Meerschweinchen mit einem durchschnittlichen Gewicht von 250 g. Die Tiere erhielten als Basisnarkotikum 10 mg Urethan/kg intraperitoneal und zusätzlich eine Ätherinhalationsnarkose. Nach Eröffnung des Abdomens wurden 2 gleich lange Jejunumabschnitte freigelegt und unter Erhaltung der Durchblutung die Darmlumen eröffnet. Zunächst wurde der Darm zur Reinigung mit Ringerlösung durchspült und anschließend in einen Darmabschnitt eine isotone 15%ige Kanamycinsulfatlösung mit einem PH von 6.8 und in den anderen ein gleich großes Volumen Ringerlösung gefüllt. Danach wurde das Darmlumen durch eine Unterbindung abgeschlossen, die Darmstücke wieder in die Bauchhöhle zurückverlagert und die Bauchdecke verschlossen. Der Darminhalt wurde nach 14 Stunden Versuchsdauer gewogen und das Gewebe zur histologischen Untersuchung in Formalinlösung fixiert, eingebettet und nach Heidenhain mit Hämatoxylin-Eosin gefärbt.

Ergebnisse

In dem Darmabschnitt, der Kanamycin enthielt, fiel, verglichen mit dem benachbarten Kontrolldarmstück, zunächst eine ausgeprägte Hyperämie auf. Der Darm erschien hochrot bis leicht bläulich verfärbt. Die gleiche Beobachtung machte Müsebeck (1962) auch am Innenohr nach SM-Intoxikationen.

Im weiteren Verlauf zeigte es sich, daß die Ringerlösung wesentlich schneller resorbiert wird. Der Resorptionsprozeß war unter Kanamycin offensichtlich gehemmt. Am Ende des Versuches war der Kanamycin enthaltende Darm fast genauso voll wie zu Beginn, während der Kontrolldarm praktisch leer war. Auf die Bestimmung des Kanamycingehaltes wurde bei diesen Untersuchungen, die lediglich orientierenden Charakter haben sollen, verzichtet, zumal die schlechte Resorbierbarkeit des Kanamycins allgemein bekannt ist.

Uns interessieren vor allem die histologischen Veränderungen an den

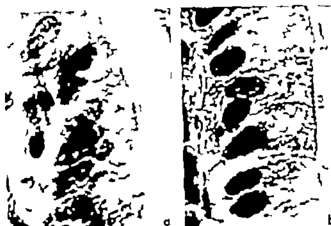


Abb 2 ( ) Darmepithelien unter Kanamycin, (*b*) Kontrolldarm (Ri gerlösung)

Darmepithelien, wie sie auf Abb 2*a* und Abb 3*a* und zum Vergleich in den Kontrolldarmabschnitten Abb 2*b* und Abb. 3*b* zu erkennen sind.

Hier zeigt sich ein sehr ähnliches Schädigungsbild, wie es bereits von den Tubuluszellen und vom Innenohr bekannt ist und übereinstimmend von zahlreichen Autoren beschrieben wurde. Die Mucosazellen waren unter Kanamycin deutlich vergrößert, *aufgetrieben und ihre Zellgrenzen nicht mehr* zu erkennen In den Zellen fanden sich große Vacuolen. Am auffälligsten war die Vergrößerung und Schwellung der Zellkerne Sie fielen außerdem durch eine intensivere Färbung und eine unregelmäßige Form auf Ein Nucleolus ließ sich nicht mehr feststellen. Demgegenüber konnten am Kontrolldarm keine pathologischen Veränderungen festgestellt werden. Die Zellkerne waren hier viel kleiner rundlich bis oval. Sie besaßen in ihrer

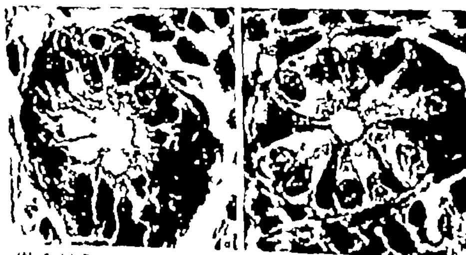


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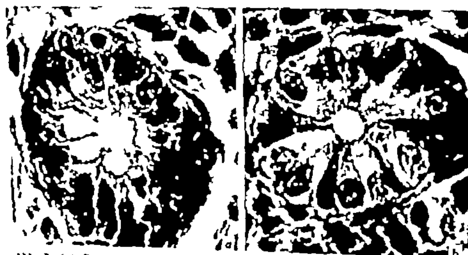


Abb. 3. ( ) Darmepithelie unter Kanamycin mit großen, intrazellulären Vacuolen. (*b*) Kontrolldarm (Ringerlösung)

Mitte einen Nucleolus und wiesen eine scharfe Begrenzung zum Zytoplasma auf

Aus diesen Untersuchungen am Darm können folgende Schlüsse gezogen werden

1 Kanamycin und wahrscheinlich auch alle anderen Streptomyceesantibiotika rufen eine allgemeine Störung der Resorptionstätigkeit hervor
2 Die Schädigung der Epithelien des Darmes erfolgt vom Lumen d h von der Mucosaseite aus und nicht auf dem Blutweg. Das bedeutet
3 Das Antibiotikum kann, obwohl es nicht resorbierbar ist dennoch vom Darmlumen aus in die oberste Zellschicht eindringen und diese schädigen
4 Die toxischen Streptomyceesantibiotika können nicht nur das Innenohr und die Niere sondern auch andere Organe wie z. B den Darm, schädigen Voraussetzung ist nur daß diese einer entsprechend hohen Kanamycinkonzentration ausgesetzt werden Mit anderen Worten die toxische Wirkung *scheint nicht in erster Linie auf einer spezifischen Sensibilität* einzelner Organe zu beruhen, sondern von der Konzentration abhängig zu sein
5 Die große Ähnlichkeit des Schädigungsbildes an den Epithelien des Darmes, der Niere und des Innenohres spricht dafür daß die Wirkungsweise der toxischen Stoffe überall die gleiche ist

Damit soll jedoch nicht gesagt sein, daß alle Zellen des Organismus die gleiche Empfindlichkeit besitzen und die Konzentration die alleinige Ursache für die Schädigung darstellt Sicher wird es auch innerhalb der Organe *das beweisen zahlreiche morphologische Untersuchungen am Innen*ohr (Kohonen, 1965 Koide *et al.*, 1966 Spoendlin 1966 u a) noch erhebliche Empfindlichkeitsunterschiede der einzelnen Zelltypen geben genauso wie man bei den bakteriologischen Resistenzbestimmungen große Unterschiede in der Sensibilität der einzelnen Erreger feststellen kann Mit zunehmender Antibiotikakonzentration wird *zwar der Kreis der emp*findlichen Keime bzw Zellen größer So wird z B eine Sinnes- oder Nervenzelle früher geschädigt werden als z. B eine Bindegewebszelle Genauso wie im Innenohr gibt es in anderen Organen ebenfalls mehr oder weniger empfindliche Zellen Wir haben keine Veranlassung anzunehmen die Epithelien oder neuralen Elemente des *Innenohres seien empfindlicher* wie häufig behauptet wird als gleichartige Zellelemente anderer Organe

In den Befunden am Darm sehen wir eine Bestätigung für unsere Annahme daß wahrscheinlich auch für die Nierenschädigungen die hohe Antibiotikakonzentration im Harn und nicht der Antibiotikaspiegel des Blutes verantwortlich zu machen ist *Die Tatsache das die toxischen Substanzen*, insbesondere in den resorptiv tätigen Organen z. B in der Niere oder dem Darm, angereichert werden, veranlaßte uns nachzuforschen, ob nicht auch im Innenohr wo ebenfalls ein *Resorptionsprozeß stattfindet* auf ähnliche Weise eine Kumulation erfolgt

Über den Streptomycingehalt des Innenohres war, wenn man von einigen Mutmaßungen absieht, bis vor kurzem nur wenig bekannt. In der Literatur findet sich lediglich eine Mitteilung von Baroni, Zanzucchi und Masera (1950). Sie verabreichten Tauben 100 mg SM-Sulfat intramuskulär und verglichen 10 min. nach der Injektion den SM-Gehalt des Blutes und der Innenohrlymphe, die aus den Bogengängen entnommen wurde. Die Bestimmung der SM-Konzentration in den Proben erfolgte auf mikrobiologischem Wege an einem Staphylokokkenteststamm. Im Blut war kein Streptomycin nachweisbar, wohl aber in der Lymphe. Man schloß hieraus, daß die Streptomycinkonzentration in der Lymphe höher sein muß als im Blut. Genauere Untersuchungen über das Verhalten der verschiedenen Aminoglykosidantibiotika im Organismus und vor allem im Innenohr wurden erst in jüngster Zeit gleichzeitig von mehreren Untersuchern durchgeführt (Muravelskaya, 1965, Stupp und Rauch, 1965, Vabree, 1965, Voldrich, 1965).

Die Ursache, warum derartige Untersuchungen erst jetzt vorgenommen wurden, ist in erster Linie in den erheblichen methodischen Schwierigkeiten, insbesondere der Endolymphgewinnung zu suchen.

IV. Vergleich der Antibiotikaspiegel im Blutserum, in den Innenohrflüssigkeiten und anderen Organen

318 Meerschweinchen mit einem durchschnittlichen Gewicht von 250 g erhielten eine einmalige subkutane Injektion eines Antibiotikums entweder aus der Oligosaccharidgruppe oder Polymyxin E (Colistin®), Tetracyclin und Penicillin G. Anschließend wurden die Antibiotikakonzentrationen über einen Zeitraum von 25 Stunden in der Peri- und Endolymphe des Innenohres und zum Vergleich im Blutserum, Herzmuskel, in der Leber, im Großhirn sowie im vestibulären Kerngebiet des Hirnstammes bestimmt. Die Messungen erfolgten 10 Minuten, 1/2, 1 Stunde, zwei, fünf, zwölf, achtzehn und fünfundzwanzig Stunden nach einer einmaligen Injektion. Für jede einzelne Bestimmung mußte jeweils ein Tier geopfert werden. Die folgende Aufstellung gibt die untersuchten Substanzen und ihre Dosierungen an. Alle Gewichte beziehen sich stets auf die Antibiotika-Base.

Antibiotikum	Dosierung
1. Kanamycin-Sulfat	250, 50, 25 und 15 mg/kg
2. Kanamycin-Monopantothenat	250 mg/kg
3. Kanamycin-Dipantothenat	250 mg/kg
4. Kanamycin-Tripantothenat	250 mg/kg
5. Streptomycin-Sulfat	250 mg/kg
6. Dihydrostreptomycin-Sulfat	250 mg/kg
7. Neomycin-Sulfat	100 mg/kg und 25 mg/kg
8. Colistin (Polymyxin E) als Methansulfonsaures-Na	1 Mill. E = 35 mg/kg
9. Tetracyclin-HCl	100 mg/kg
10. Penicillin G	400 000 E = 240 mg/kg

Methode

Zur Gewinnung der Endo- und Perilymphflüssigkeit mußten die Meerschweinchen dekapitiert werden. Anschließend wurde die Bulla in wenigen Sekunden freipräpariert, weit eröffnet, damit die Cochlea gut zugänglich wird, und sofort in flüssigem Stickstoff eingefroren. In einer Tiefkühlkammer bei −2‹ erfolgte dann unter einem Operationsmikroskop (Zeiss) die Entfernung der knöchernen Kapsel der Schnecke mit Hilfe einer Fräse. Nach der von Rauch beschriebenen Technik (s. Biochemie des Innenohres, Thieme Verlag) läßt sich dann die Perilymphe der Scala vestibuli und tympani sowie die Endolymphe des Ductus cochlearis in den einzelnen Windungen der Schnecke in kleinen Bruchstücken voneinander trennen. Die aus einer Schnecke gewonnene Endolymphmenge betrug maximal 1,2/µl. Da zur bakteriologischen Messung des Antibiotikagehaltes bzw. genauer gesagt der antibiotischen Aktivität relativ große Lymphmengen erforderlich waren, mußten stets die Endolymphen von 3–6 Tieren zusammengenommen und ausgewertet werden. Evtl. Blutbeimischungen ließen sich durch eine photometrische Hb-Bestimmung feststellen und berechnen.

Aus verständlichen methodischen Gründen konnte nicht in allen Fällen *die Endolymphpräparation durchgeführt werden. Die Perilymphgewinnung* bereitete demgegenüber keine besonderen Schwierigkeiten. Sie konnte am lebenden Tier in Urethan-Äthernarkose durchgeführt werden. Die Bulla wurde hierbei freipräpariert, eröffnet und mit einer Nadel ein kleines Bohrloch zur Scala vestibuli der unteren Schneckenwindung angebracht. Aus dieser Öffnung konnte mit einer dünnen *ausgezogenen Glaskapillare durch* Adhaesion Perilymphe aus der Scala vestibuli abgezogen werden. Die Lymphflüssigkeit wurde in kleinen gut verschließbaren Polyaethylenspitz

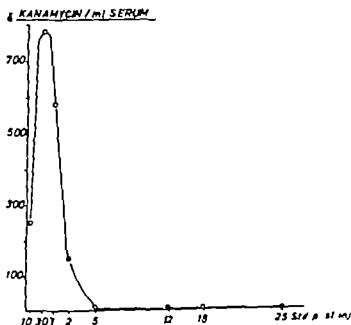


Abb. 3. Blutspiegel nach ... 250 mg Kanamycin ... bezog. auf di Kanamycin Base

behältern gesammelt und die Lymphmenge auf der Mikrowaage bestimmt. Aus einer Cochlea wurden durchschnittlich 0,5–1,2/µl Endo- und 5/µl Perilymphe gewonnen.

Die Bestimmung des Antibiotikagehaltes erfolgte auf bakteriologischem Wege durch Messung der antibiotischen Aktivität. Es wurde das allgemein in der Bakteriologie übliche Agardiffusionsverfahren angewendet, und zwar bei Seren und Geweben in Form des Lochtestes und bei den Lymphen mit Hilfe des Blättchentestes. Verwendet wurden Filterblättchen Nr. 22 (Schleicher & Schüller) mit einem Durchmesser von 5 mm. Als Teststamm diente Bact. subtilis ATCC 6633. Die niedrigste feststellbare Kanamycinkonzentration betrug im Serum und Gewebe 0.01 γ/ml bzw. 0.01 γ/g Frischgewicht, in der Innenohrlymphe 0,5 γ/ml. Die niedrigste feststellbare Neomycindosis betrug 1 γ/ml in Serum und Organen, aber nur 5 γ/ml in der Innenohrlymphe. Die Nachweisgrenzen für Colistin lagen bei 0.01 bzw. für die Lymphe bei 3 γ/ml, für Penicillin bei 0.01 IE/ml bzw. 0,2 IE/ml Lymphe.

Die mittlere Abweichung und die statistische Signifikanz der gemessenen Werte wurden hier wie auch bei den folgenden Versuchen unter Berücksichtigung der Anzahl der Versuche ($N < 100$) nach der T-Verteilung ermittelt.

Ergebnisse

Im Verhalten der Streptomycesantibiotika im Blutserum und in der Perilymphe des Innenohres lassen sich einige bemerkenswerte Unterschiede feststellen. Unmittelbar nach einer subkutanen Injektion von 250 mg Kanamycin/kg kommt es zu einem sehr schnellen Anstieg des Blutspiegels.

Die Serumkonzentration des Kanamycins betrug bereits nach 10 min 250 γ/ml und erreichte schon nach 1/2 Stunde ihr Maximum mit 800 γ/ml. Fast genauso schnell wie der Anstieg erfolgte auch die Eliminierung des Kanamycins aus dem Blut. 1 Stunde nach der Injektion war bereits eine deutliche Abnahme des Blutserumspiegels feststellbar. Die Halbwertzeit des Kanamycins im Blut betrug nur 85 min. Dieser Wert stimmt mit den Angaben anderer Autoren überein. Sous (zit. bei Mückter 1961) fand für Dihydrostreptomycin beim Kaninchen eine Halbwertzeit von 80 min und Dost (1953) beim Menschen von 72 min.

In den Innenohrflüssigkeiten verhält sich Kanamycin dagegen ganz anders.

Abb. 5 zeigt zum Vergleich die Kanamycinspiegel des Serums und der Innenohrflüssigkeiten. Entgegen den bisherigen Vorstellungen erreicht Kanamycin im Innenohr überraschend hohe Konzentrationen. Bei einem Vergleich der Kanamycinkonzentrationskurven des Blutes und des Innenohres muß man feststellen, daß offenbar keine direkte Abhängigkeit vom Blutspiegel zu bestehen scheint. Es sieht so aus, als herrschten im Innenohr sowohl hinsichtlich der Anreicherung als auch bei der Ausscheidung des Kanamycins andere Gesetzmäßigkeiten vor. Im Gegensatz zu dem schnellen Anstieg des Blutspiegels nimmt die Kanamycinkonzentration der Innenohr

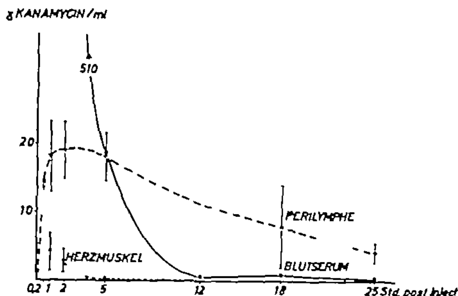


Abb 5 Kanamycinspiegel im Serum, in der Perilymphe und im Herzmuskel nach einmaliger Injektion, 250 mg/kg. (Alle Werte beziehen sich auf die Kanamycin Base)

flüssigkeiten auffallend langsam zu Kanamycinsulfat erreicht hier erst nach 1–2 Stunden, andere Antibiotika der Aminoglykosidgruppe wie Streptomycin oder die verschiedenen Pantothenatsalze des Kanamycins, auf die anschließend näher eingegangen werden soll sogar noch später nach 2–5 Stunden ihren höchsten Wert zu einem Zeitpunkt also, wo bereits ein wesentlicher Teil des Antibiotikums wieder aus dem Blut eliminiert ist

Noch mehr als der Anreicherungsprozeß verdient vor allem der verzögerte Abtransport der toxischen Substanzen aus dem Innenohr Beachtung Während der Kanamycinspiegel im Blutserum sehr schnell sinkt bleiben die hohen Kanamycinkonzentrationen in den Innenohrflüssigkeiten über eine erstaunlich lange Zeit erhalten Sie zeigen nur eine geringe Tendenz zur Abnahme Die Halbwertzeit des Kanamycins ist im Innenohr mit annähernd 15 Stunden 10 mal länger als im Blut Wie aus der Abb 5 zu erkennen ist, war der Kanamycinspiegel im Blutserum nur verhältnismäßig kurze Zeit wesentlich höher als in den Innenohrflüssigkeiten Bereits 5 Stunden post inj enthielt das Innenohr fast 3 mal soviel und nach 25 Stunden sogar 15 mal soviel Kanamycin wie das Blutserum Die Abb 5 zeigt deutlich die viel flacher verlaufende Ausscheidungskurve des Kanamycins in der Perilymphe welche die steil abfallende Blutkonzentrationskurve in charakteristischer Weise überschneidet Dieser Kurvenverlauf kann als ein typisches Zeichen für einen Kumulations bzw Retentionsprozeß im Innenohr angesehen werden

Wie extrem hoch der Kanamycingehalt der Innenohrflüssigkeiten in Wirklichkeit ist kommt am besten bei einem Vergleich mit anderen Organen zum Ausdruck (Tab 1) 5 Stunden nach einer einmaligen subkutanen Injektion von 250 mg Kanamycin/kg fand sich in den Innenohr-

TABELLE 1. *Vergleich des Kanamycingehaltes verschiedener Organe*

Std. post inject	Perilymphe	Endolymphe	Serum	Herz	Leber	Hirnstamm	Großhirn
5	23,5	16	9,2	0,71	0,65	0,150	0,124
18	12,0	11	0,7	0,44	0,39	0,10	0,055

γ Kanamycin-Base/ml bzw. g Organ (Frischgewicht)

flüssigkeiten z. B. 20 mal soviel Kanamycin wie im Herz, 30 mal soviel wie in der Leber und über 100 mal mehr als im Gehirn.

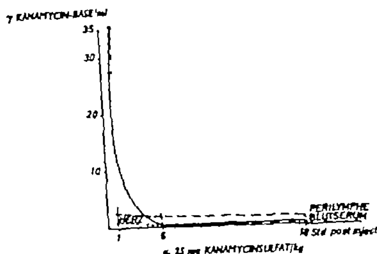
Dieses Verhältnis verschiebt sich 18 Stunden post inj. bemerkenswerter weise noch weiter zugunsten der Innenohrlymphe. Zu diesem Zeitpunkt ist die Kanamycinkonzentration, wie aus der Tabelle hervorgeht, fast 50 mal so hoch wie im Herz und in der Leber und sogar 500 mal höher als im Gehirn. Das bedeutet, der Abtransport des Kanamycins aus dem Innenohr erfolgt trotz der hohen Konzentration und des günstigeren Diffusionsgefälles zum Blut und den benachbarten Geweben hin langsamer als die Eliminierung der geringen Kanamycinspuren aus den übrigen Organen.

Man könnte hier einwenden, daß ein derartiger Vergleich zwischen Innenohrflüssigkeiten und anderen Organen nicht möglich ist. Zwar repräsentiert die Innenohrlymphe, die mehr als 90% des gesamten Innenohres ausmacht, praktisch volumenmäßig das Innenohrorgan. Das Verhältnis Extrazellularraum zu zellulären Elementen ist im Innenohr jedoch besonders extrem zugunsten der extrazellulären Flüssigkeiten verschoben. Da die Streptomycesantibiotika, wie bereits erwähnt wurde, überwiegend extrazellulär vorkommen, könnte die hohe Antibiotikakonzentration im Innenohr allein schon durch den großen Extrazellularraum des Innenohres erklärt werden. Genauso liesse sich der geringe Antibiotikagehalt der Organe auf ihren verhältnismäßig kleinen extrazellulären Raum zurückführen. Nach Cardozo und Edelman (Thiosulfatmethode) macht das gesamte extrazelluläre Wasser 16,6% des Körpergewichtes aus, nach Levitt und Gaudino (Inulinmethode) 15%. Demnach enthalten z. B. Herz oder Leber nur etwa 1/6 soviel Wasser wie das Innenohr. Diese Organe müssen daher zwangsläufig entsprechend weniger Kanamycin enthalten. Aber selbst bei Berücksichtigung dieser Relation Extrazellularraum zur Zelle bleibt die Antibiotikakonzentration im Innenohr immer noch um ein vielfaches höher als in anderen Organen, vor allem wenn der Blutgehalt der Organe noch berücksichtigt wird.

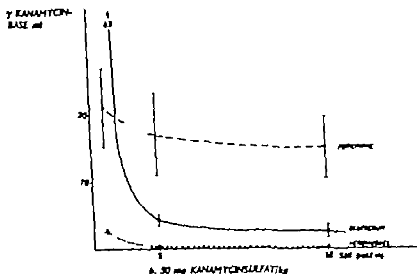
Besonderes Interesse verdient der erhebliche Unterschied zwischen dem Kanamycingehalt der Perilymphe und des ZNS. Im Großhirn und vestibulären Kerngebiet des Hirnstammes konnten im Vergleich zum Innenohr nur Spuren von Kanamycin nachgewiesen werden. Vor allem war auch kein Unterschied zwischen dem Kanamycingehalt des Großhirns und des

Hirnstammgebietes erkennbar. Diesem Befund kommt im Hinblick auf die gegensätzlichen Auffassungen über den Schädigungsort der Streptomycessubstanzen besondere Bedeutung zu. Wie bereits erwähnt wurde, nehmen einige Untersucher eine zentrale Schädigung im Kerngebiet an. Nach Ansicht der meisten Autoren allerdings ist der primäre Angriffsort überwiegend oder sogar ausschließlich im peripheren Sinnesapparat zu suchen. Nur bei extrem hohen Dosierungen lassen sich im ZNS morphologisch faßbare Veränderungen erkennen. Die letztere Auffassung findet durch unsere Untersuchungen eine weitere Stütze. Der hundertfach höhere Kanamycinspiegel des Innenohres spricht für eine primäre Schädigung des peripheren Hör- und Gleichgewichtsorganes. Kanamycin war im Gehirn nur in so geringen Mengen vorhanden, die kaum in der Lage sein dürften, hier Schädigungen hervorzurufen. Insbesondere wiesen auch die angeblich bevorzugt geschädigten Kerngebiete keinen höheren Kanamycingehalt auf, der eine bevorzugte Intoxikation dieses Hirnabschnittes erklären könnte.

Um über den Intoxikationsmechanismus eine genauere Aussage machen zu können, genügte nicht nur die Bestimmung des Kanamycins in der Perilymphe. Vor allem war es entscheidend zu wissen, wieviel Kanamycin in die Endolymphe und damit in unmittelbaren Kontakt mit dem Cortiorgan gelangt. Diese Frage ist insofern berechtigt, da Perilymphe und Endolymphe durch die Reissnersche Membran vollständig von einander getrennt sind und bekanntlich erhebliche Unterschiede z. B. in ihrer Ionenzusammensetzung aufweisen. So enthält die Perilymphe überwiegend Natrium und nur wenig Kalium, während die Endolymphe umgekehrt sehr viel Kalium aber nur wenig Natrium besitzt. Aus diesem Grunde war der große Arbeitsaufwand, der mit der Endolymphgewinnung verbunden ist, für eine genaue Klärung der ototoxischen Wirkung unumgänglich. Überraschenderweise zeigte es sich aber, daß der Kanamycingehalt der Endolymphe stets weitgehend dem der Perilymphe entsprach. Geringe Konzentrationsunterschiede lagen im normalen Schwankungsbereich der angewandten Untersuchungsmethoden und ließen sich statistisch nicht sichern. Die auffallende Übereinstimmung der Kanamycinkonzentrationen in der Peri- und Endolymphe könnte ein Hinweis dafür sein, daß wahrscheinlich eine Diffusion durch die Reissnersche Membran hindurch stattfindet, die zu einem Konzentrationsausgleich führt. Die unterschiedlichen Kalium- und Natriumkonzentrationen in der Peri- und Endolymphflüssigkeit schließen einen Diffusionsvorgang nicht unbedingt aus. Es ist durchaus vorstellbar, daß in den Lymphräumen neben einem sog. aktiven Transport auch passive Diffusionsvorgängen stattfinden. Der Kalium- und Natriumtransport und damit der Aufbau des Endolymphpotentials beruht wahrscheinlich auf dem bekannten Mechanismus der K-Na-Pumpe, also auf einer aktiven Zelleistung. Die ausschließlich extrazellulär vorkommenden unphysiologischen Substanzen wie die Streptomycesantibiotika müssen dagegen auf einem anderen Wege, wahrscheinlich über die Interzellularspalten die Reissnersche Membran passieren. Dieser Permeationsvorgang scheint von der Zellfunk-



a. 25 mg KANAMYCINSULFAT/kg



b. 50 mg KANAMYCINSULFAT/kg

Abb. 6 a und b Vergleich der Kanamycinspiegel im Blutserum, Herzmuskel und in der Perilymphe bei verschiedenen Dosierungen. (Alle Werte beziehen sich auf die Kanamycin-Base.)

tion unabhängig zu sein und nur den Gesetzen der Diffusion zu unterliegen.

Mit der hohen Konzentration und der langen Verweildauer der toxischen Substanzen vor allem auch in der Endolymphe sind alle Voraussetzungen für eine direkte Einwirkung auf die Sinneszellen des Innenohres erfüllt.

V. Die Beziehung zwischen der Kanamycindosis und den Blut-, Gewebs- und Innenohrspiegeln

Die bisherigen Untersuchungen wurden mit relativ hohen und sicher toxischen Kanamycindosen von 230 mg/kg durchgeführt. Diese für das Tier

Hirnstammgebietes erkennbar. Diesem Befund kommt im Hinblick auf die gegensätzlichen Auffassungen über den Schädigungsort der Streptomyces-substanzen besondere Bedeutung zu. Wie bereits erwähnt wurde, nehmen einige Untersucher eine zentrale Schädigung im Kerngebiet an. Nach Ansicht der meisten Autoren allerdings ist der primäre Angriffsort überwiegend oder sogar ausschließlich im peripheren Sinnesapparat zu suchen. Nur bei extrem hohen Dosierungen lassen sich im ZNS morphologisch faßbare Veränderungen erkennen. Die letztere Auffassung findet durch unsere Untersuchungen eine weitere Stütze. Der hundertfach höhere Kanamycinspiegel des Innenohres spricht für eine primäre Schädigung des peripheren Hör- und Gleichgewichtsorganes. Kanamycin war im Gehirn nur in so geringen Mengen vorhanden, die kaum in der Lage sein dürften, hier Schädigungen hervorzurufen. Insbesondere wiesen auch die angeblich bevorzugt geschädigten Kerngebiete keinen höheren Kanamycingehalt auf, der eine bevorzugte Intoxikation dieses Hirnabschnittes erklären könnte.

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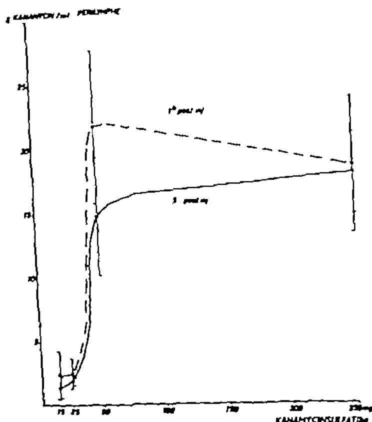


Abb. 7 Beziehung zwischen Kanamycindosis und Kanamycinkonzentration in der Perilymphe (Alle Werte beziehen sich auf die Kanamycin-Base.)

Eine nochmalige Steigerung der Dosis sogar um das 5-fache auf 250 mg/kg, führt, wie die folgende Abb. 7 zeigt, nur noch zu einem entsprechenden Anstieg des Blut- und Gewebsspiegels. Trotz des 5 mal so hohen Blutspiegels nahm jetzt die Konzentration des Kanamycins im Innenohr nicht mehr weiter zu. Es sieht so aus, als käme der Anreicherungsprozeß für Kanamycin im Innenohr mit zunehmender Dosierung nach einem anfänglichen kurzen aber steilen Anstieg zum Stillstand. Das Verhältnis Kanamycindosis zur Kanamycinanreicherung im Innenohr wird durch eine steile Sättigungskurve charakterisiert. Dagegen scheint zwischen der applizierten Dosis und dem Blutspiegel nur eine einfache lineare Beziehung zu bestehen (Abb. 8)

Dieser Befund fordert zu mehr oder weniger spekulativen Betrachtungen heraus, auf die später noch eingegangen werden soll. Er ist darüber hinaus auch für die praktische Anwendung und Dosierung der Streptomycesantibiotika von Bedeutung, weil er zeigt, wie gerade in dem therapeutisch in Betracht kommenden Dosisbereich schon geringfügige Dosiserhö-

experiment übliche Dosierung ist aber wie man mit Recht einwendet therapeutisch uninteressant Für die Praxis ist es vielmehr von Bedeutung, zu wissen wie sich Kanamycin im therapeutischen Dosisbereich verhält oder welche Folgen eine längere Behandlung hat

1 Die Bedeutung der Ein eldosis für die Blut und Organkon entration

Betrachten wir zunächst die Beziehung zwischen der Höhe der Kanamycindosis und den Blut Gewebs und den Innenohrspiegeln Durch eine einmalige Gabe von nur 15 mg Kanamycin/kg läßt sich ein Blutspiegel von ungefähr 20 γ/ml Blutserum erzielen Eine Erhöhung der Dosis auf 25 mg/kg führt wie die Abb 6 zeigt, zu einer entsprechenden Erhöhung der Blutkonzentration auf 36 γ/ml

Ebenso und offensichtlich in Abhängigkeit vom Blutspiegel nimmt auch der Kanamycingehalt der Organe zu wenn auch die Gewebsspiegel vergleichsweise sehr gering sind Die Kanamycinkonzentration im Herzmuskel erreichte nicht einmal 1 γ/g, wobei sicher noch der größte Anteil auf den hohen Blutgehalt dieses Organes zurückzuführen ist In der Leber fand sich nur 1/10 davon, also 0 1 γ/g, ein Wert der auf dieser Abb nicht mehr darzustellen war Im Gehirn konnte überhaupt kein Kanamycin festgestellt werden, d h., die Konzentration lag unter der Nachweisgrenze von 0 01 γ/g. Nur die Innenohrflüssigkeiten wiesen schon bei einer Dosierung von 15 mg/kg 2,0 γ/ml und bei 25 mg/kg 2,5 γ/ml Perilymphe auf Dieser relativ hohe Kanamycingehalt der Innenohrflüssigkeit ist umso beachtenswerter wenn man außerdem die Halbwertzeit im Innenohr berücksichtigt, die länger ist als in allen anderen Organen und vor allem auch viel länger als im Blut. Während Kanamycin z. B 5 Stunden post inj wieder weitgehend bis auf einen geringen Rest von 0 14 γ/ml aus dem Blut eliminiert war betrug der Kanamycingehalt der Innenohrflüssigkeiten zu diesem Zeitpunkt immer noch 1 9 γ/ml und übertraf damit den Blutspiegel um mehr als das 10-fache. Es fällt also schon bei niedrigen Dosen eine Anreicherung bzw Retention des Kanamycins im Innenohr auf

Wir hatten bereits auf das unterschiedliche Verhalten des Kanamycins im Blutserum und in den Innenohrflüssigkeiten hingewiesen und hieraus den Schluß gezogen daß im Innenohr wahrscheinlich ein besonderer Mechanismus vorliegen muß der sowohl für den deutlichen langsameren Anreicherungsprozeß als auch für den erheblich verzögerten Abtransport aus den Innenohrräumen verantwortlich ist. Dieses eigentümliche Verhalten der Streptomycesantibiotika kam bei weiteren Versuchen noch deutlicher zum Ausdruck.

Erhöht man nämlich die Kanamycindosis von 25 mg/kg auf 50 mg/kg, so zeigt sich zwar erwartungsgemäß ein doppelt so hoher Blutspiegel und auch eine entsprechende Erhöhung der Kanamycinkonzentration im Gewebe z B des Herzmuskels wie auf der Abb 6 a zu sehen ist Überraschenderweise stieg aber der Kanamycingehalt der Perilymphe viel stärker ja geradezu sprunghaft um ungefähr das 10-fache an

weiteren signifikanten Zunahme der Innenohrkonzentration um insgesamt 137% vom Ausgangswert. Hier zeigt sich eine interessante Erklärung für eine aus der Praxis längst bekannte Erfahrungstatsache. Die besondere Gefahr bei einer Langzeitbehandlung mit Streptomycesantibiotika beruht demnach nicht etwa auf einer einfachen Summation der Schädigungen, sondern wahrscheinlich in erster Linie auf der Tatsache, daß mit jeder weiteren Injektion das jeweilige Maximum des Innenohrspiegels langsam aber stetig zunimmt.

Für den Anstieg der Innenohrkonzentration bei gleichbleibender Dosierung kommen verschiedene Ursachen in Betracht. Zunächst muß eine renal bedingte Ausscheidungsstörung z. B. infolge einer toxischen Nierenschädigung ausgeschlossen werden. Dieser Fehler unterlief z. B. Voldrich, als er ähnliche Untersuchungen mit dem besonders oto- und nephrotoxischen Neomycin durchführte und dabei schon nach wenigen Injektionen extrem hohe Innenohrspiegel fand. Tatsächlich handelte es sich hier aber wie wir nachweisen konnten, nicht um einen organspezifischen Anreicherungsprozeß, sondern um eine Störung der renalen Ausscheidung. Als Ausdruck einer gestörten Nierenfunktionen bleiben die Blutspiegel, die normalerweise schon nach einer halben Stunde wieder abnehmen, unter Neomycin während der ganzen Versuchsdauer auf ihrer maximalen Höhe bestehen. Daß unter diesen Bedingungen hohe Innenohrkonzentrationen auftreten, die genauso lange andauern wie der Blutspiegel, ist daher nicht weiter verwunderlich. — Bei den oben geschilderten Dauerbehandlungen mit Kanamycin wurde jedoch weder der Blut- noch der Gewebsspiegel in irgend einer Weise beeinflußt. Sie verhielten sich nach 20 Injektionen genau wie nach der ersten. Eine renale Ausscheidungsstörung kann also hier nicht zur Erklärung herangezogen werden.

Als nächstes mußte man daran denken, daß vielleicht die erheblich verzögerte Ausscheidung des Kanamycins für die Konzentrationszunahme bei einer Dauerbehandlung verantwortlich ist. Die Eliminierung des Kanamycins ist wie auch aus der Abb. 5 hervorgeht, nach 25 Stunden bei weitem noch nicht abgeschlossen. Es finden sich am nächsten Tage, an dem in üblicher Weise bereits die nächste Injektion erfolgt, noch ungefähr 10% des Kanamycin vom Vortage in den Innenohrflüssigkeiten. Eine 2. Injektion muß daher zwangsläufig zu einem höheren Innenohrspiegel führen. Durch einen stetig wachsenden Rückstau an Kanamycin würde somit die Kumulation eine Erklärung finden. Es stellte sich aber heraus, daß mit steigender Innenohrkonzentration die Kanamycinrückstände im Innenohr nicht in dem Maße, wie man es erwarten sollte zunehmen. Vielmehr zeigte es sich, daß je höher die Innenohrkonzentration ist, umso schneller auch die Ausscheidung erfolgt. Das bedeutet, mit steigendem Kanamycingehalt im Innenohr nimmt die ausgeschiedene Kanamycinmenge pro Zeiteinheit zu, so daß eine fortschreitende Retention der toxischen Substanzen, wie es die Abb. 9 zeigt, weitgehend verhindert wird. Nach 18 bzw. 25 Stunden post inj. erreicht der Perilymphspiegel, auch wenn er wesentlich höher war

4 921043 Progr

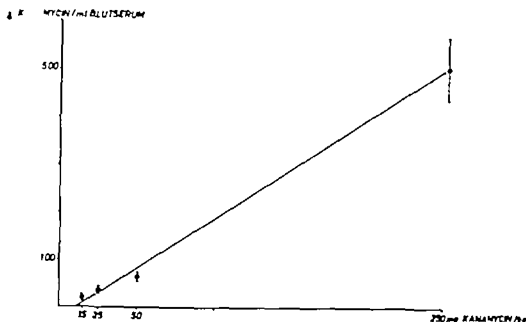


Abb. 8. Beziehung zwischen Kanamycindosis und Kanamycin-Blutkonzentration.

hungen einen unverhältnismäßig hohen Anstieg der Antibiotikakonzentration im Innenohr zur Folge haben. Diese plötzliche Zunahme des Antibiotikagehaltes stellt wahrscheinlich die toxische Schwelle des Innenohres dar. Die kritische Schwellendosis liegt – dessen sollte man sich stets bei einer Behandlung mit den toxischen Streptomycesantibiotika bewußt sein – noch im sog. therapeutischen Bereich. Die klinisch schon lange bekannte Tatsache, daß die therapeutische Breite dieser Substanzgruppe außerordentlich gering ist, findet durch diesen Befund ihre Bestätigung und Erklärung.

2. *Der Einfluß einer Dauerbehandlung mit Streptomycesantibiotika auf die Blut-, Gewebs- und Innenohrspiegel*

Obwohl der Perilymphspiegel schon nach einer einmaligen Injektion von 250 mg/kg Kanamycin einen Höchstwert erreicht zu haben schien, zeigte es sich, daß das Innenohr unter bestimmten Umständen in der Lage ist, noch mehr Kanamycin aufzunehmen. Verabfolgt man die gleiche Kanamycindosis 10 oder 20 mal in täglichen Abständen, so kann man, wie Abb. 9 zeigt, eine weitere erhebliche Steigerung der Kanamycinkonzentration erzielen.

Die Zunahme mag zwar verglichen mit dem steilen Anstieg im niedrigen Dosisbereich, wie wir es oben sahen, relativ gering erscheinen. Der absolute Zuwachs ist trotzdem beachtenswert und sicher auch in toxischer Hinsicht nicht bedeutungslos. Nach einer 10 tägigen Behandlung mit einer Tagesdosis von 250 mg/kg konnten wir einen statistisch zu sichernden Anstieg des Kanamycingehaltes in den *Innenohrflüssigkeiten* von 50 % feststellen. Nach 20 Injektionen der gleichen Dosis kam es nochmals zu einer

VI Zur Ursache der Anreicherung und verzögerten Ausscheidung der Aminoglykosidantibiotika

Bevor wir uns der Frage zuwenden, warum die toxischen Substanzen ausgerechnet im Innenohr angereichert werden, muß man sich zunächst einmal die Frage stellen, wie sich normalerweise andere Stoffe, seien es solche mit guten oder schlechten Resorptionseigenschaften, im Innenohr verhalten.

Bereits Portmann, Geraud, Morin, Kaneko und Blanquet (1960) und Rauch (1960) machten die Feststellung, daß markiertes Natrium nach intravenöser Injektion relativ schnell in die Perilymphe des Innenohres gelangt, seine Entfernung aus den Innenohrräumen aber verglichen mit dem Blutspiegel deutlich verzögert ist. So kommt es, daß die Perilymphe einige Stunden nach der Injektion bis zu 1,75 mal soviel Na^{2} enthält wie das Blut. Dieses Verhältnis zwischen Blut und Perilymphe bleibt über 48 Stunden konstant. Es stellt sich also ein Gleichgewicht zwischen Blut und Innenohrflüssigkeit ein.

Ähnliche Versuche führte Schreiner mit P^{32}-markiertem Phosphat (1961) und mit J^{131}-markiertem Albumin (1966) durch. Hierbei zeigte sich aber, daß der Perilymphspiegel der Phosphate und auch des Albumins stets erheblich unter der Blutkonzentration lag. Die Ionen scheinen in dieser Hinsicht eine Ausnahme zu machen.

In Anbetracht der großen Unterschiede, die diese Substanzen sowohl in biochemischer als auch in physiologischer Hinsicht aufweisen, ist eine Deutung der Befunde sehr schwierig. Bei der Verteilung dieser Stoffe im Organismus und auch im Innenohr müssen verschiedene Faktoren, wie z. B. ihre Reaktionsfähigkeit und ihr Stoffwechsel, ihre Molekülgröße und ihre unterschiedlichen Permeationsmöglichkeiten, seien es aktiver Transport oder passive Vorgänge, berücksichtigt werden.

1 *Die Untersuchung der Inulinclearance des Innenohres*

Um eine genauere Aussage über den Stoffaustausch in den Innenohrflüssigkeiten machen zu können, war es daher erforderlich, Substanzen zu verwenden, die sich durch genau definierte und überschaubare Eigenschaften auszeichnen. Es lag nahe, solche Substanzen für die Untersuchung im Innenohr heranzuziehen, wie sie auch bei Clearenceuntersuchungen der Niere Anwendung finden. Wir wählten hier das Inulin, das den Vorteil hat, weitgehend chemisch indifferent und sehr stabil zu sein. Darüber hinaus besitzt Inulin als Substanz des extrazellulären Raumes den Vorzug, weder resorbiert noch sezerniert zu werden. Für die Verteilung des Inulins im Organismus kommen nur Filtrations- und Diffusionsvorgänge in Betracht. Auf Grund dieser Eigenschaften hat Inulin eine große Bedeutung zur Bestimmung des Extrazellularraumes und der Filtrationsgröße der Niere erlangt. Bei unseren Versuchen erwarteten wir vom Inulin Aufschluß darüber, ob und in welchem Ausmaß Diffusions- und Filtrationsvor

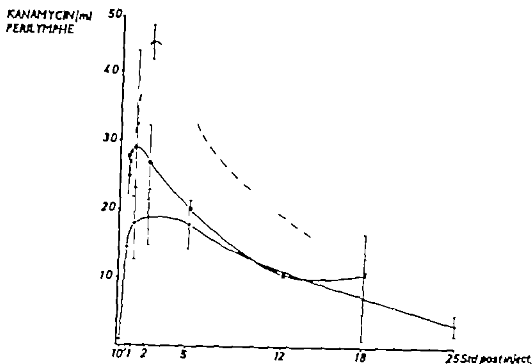


Abb. 9. Kanamycinspiegel in der Perilymphe nach 1 (—x—), nach 10 (—O—) und 20 (— — ● — —) täglichen Injektionen von 250 mg Kanamycinsulfat/kg. (Alle Werte beziehen sich auf die Kanamycin-Base.)

annähernd wieder den gleichen Ausgangswert. Die Abhängigkeit der Ausscheidungsgeschwindigkeit vom Konzentrationsgefälle spricht dafür, daß die Eliminierung der Streptomycesantibiotika wahrscheinlich nach den Gesetzen der Diffusion vor sich geht.

Der außergewöhnlich langsam verlaufende Abtransport der toxischen Substanzen aus dem Innenohr kann demnach nicht allein für die zunehmende Konzentration bei einer Dauerbehandlung verantwortlich sein. Vielmehr scheint ein Zusammenhang zwischen der fortschreitenden Intoxikation und dem Anstieg der Kanamycinkonzentration zu bestehen. Vor allem sind hier toxische Schädigungen an den Innenohrmembranen in Erwägung zu ziehen, die möglicherweise den Anreicherungsprozeß des Kanamycins mit begünstigen. Man muß hier, i. G. zu den anfangs erwähnten Untersuchungen, wo lediglich eine einmalige Injektion verabreicht wurde, bedenken, daß wir bei einer Dauerbehandlung mit mehr oder weniger vorgeschädigten Membranen zu rechnen haben. Es ist anzunehmen, daß nach 24 Stunden, wenn die nächste Injektion erfolgt, noch Membranpermeabilitätsstörungen vorliegen, die eine Anreicherung des Kanamycins fördern. Die steigende Konzentration im Verlauf der Behandlung wäre demnach Ausdruck einer zunehmenden toxischen Schädigung des Innenohres. Es liegt hier offenbar ein Circulus vitiosus vor. Je höher der Kanamycinspiegel im Innenohr, umso ausgeprägter sind die toxischen Schädigungen. Je stärker aber die Schädigung, umso mehr Kanamycin wird wiederum angereichert.

erfolgte auf die übliche, bereits beschriebene Weise in der Tiefkühlkammer. Nach Homogenisierung und Aufbereitung des Materials mit Hyamin hydroxyd in einem kochenden Wasserbad und anschließender Zugabe von Diolal erfolgte die Messung in einem Tricarb-Scintillationszähler. Der hier bei entstehende Quentsch Effekt ließ sich anhand einer Eichkurve eliminieren. Die gemessene Impulszahl pro Minute wurde auf das Frischgewicht der Organe bezogen.

Wie Abb. 10 zeigt, gelangt Inulin trotz seines hohen Molekulargewichtes von 6000 offensichtlich ohne Schwierigkeiten in das Innenohr. Das bedeutet, da eine Sekretion ausgeschlossen werden kann, daß der Eintritt in die Innenohrräume entweder durch Filtration oder über eine Diffusion erfolgen muß. Dieser Befund ist für die Physiologie des Innenohres von Interesse, da bis in die jüngste Zeit hinein die Auffassung vorherrschte, daß die Innenohrflüssigkeiten ein Sekretionsprodukt z. B. der Stria vascularis darstellen. Die Inulinversuche sprechen vielmehr für die neuerdings von Schindler wiederaufgegriffene Theorie, wonach zumindest die Perilymphe als ein Ultrafiltrat des Blutes anzusehen ist. In Anbetracht des etwa gleich hohen Inulingehaltes der Endolymphe drängt sich die Frage auf, ob nicht auch für die Endolymphbildung Filtrationsvorgänge oder eine Diffusion aus dem Perilymphraum durch die Reissner'sche Membran verantwortlich sind.

Der Inulinversuch vermittelt nicht nur einen Einblick in die Entstehung der Innenohrflüssigkeiten, sondern darüberhinaus auch in ihren Austausch. Die nicht resorbierbaren Stoffe wie Inulin gelangen zwar leicht in die Innenohrräume, aber offensichtlich nur schwer wieder heraus. Verglichen mit anderen gut resorbierbaren Stoffen bleibt Inulin viel länger im Innenohr zurück und erreicht hier Konzentrationen, die mehr als das Doppelte des Blutspiegels ausmachen. Die Anreicherung des Inulins kann wahrscheinlich darauf zurückgeführt werden, daß es aus dem Innenohr nicht aktiv rückresorbiert wird, sondern nur diffundieren kann. Demgegenüber scheinen gut resorbierbare Stoffe leichter eliminierbar zu sein, da sie zusätzlich der aktiven Rückresorption durch die Zellen der Stria vascularis oder des Ductus endolymphaticus unterliegen. Dieser Ausweg aus dem Innenohr steht dem Inulin nicht zur Verfügung. Das Verhalten des Inulins, das man auch als Inulinclearance des Innenohres bezeichnen könnte, zeigt, wie weit ein *Stoffaustausch* im Innenohr allein durch Filtration und Diffusion und *unabhängig von aktiven Resorptions-* und Sekretionsprozessen möglich ist.

Die Kumulation der Aminoglykosidantibiotika im Innenohr

Darüberhinaus bringen uns die Inulinbefunde auch einer Erklärung der Kumulationsvorgänge bei den Streptomycinantibiotika näher. Kanamycin z. B. erreicht, wie oben bereits gezeigt wurde, in einer niedrigen Dosierung von 15 oder 25 mg/kg, die praktisch aequimolar ist mit der oben angewandten Inulindosis, einen mit Inulin vergleichbaren Innenohrspiegel. Er beträgt ebenfalls 5 Stunden post inj. das 2,5-fache des Blutspiegels und

gange für den Stoffaustausch in den Innenohrflüssigkeiten in Betracht kommen.

Neben diesen physiologischen Aspekten eignet sich Inulin im Rahmen unserer Untersuchungen deswegen ganz besonders gut, da es sehr ähnliche Eigenschaften aufweist wie die Aminoglykosidantibiotika. Daß beide chemisch Zuckerverbindungen darstellen, sei hier nur am Rande bemerkt. Ein Vergleich des Inulins mit den Aminoglykosidantibiotika ist vor allem deswegen aufschlußreich, weil beide Substanzen bemerkenswerterweise die gleichen Permeationseigenschaften besitzen.

Methode

Für die Untersuchungen verwendeten wir C^{14}-markiertes Inulin-Carboxyl, das Meerschweinchen subkutan injiziert wurde. Wegen der außerordentlich kleinen Verhältnisse im Innenohr war es erforderlich, um eine meßbare Menge zu erzielen, hohe Dosen von 35 mg Inulin mit einer Gesamtaktivität von 0,1 mC pro Tier zu verabreichen. Wegen der hohen Kosten mußte auf eine größere Versuchsserie verzichtet werden.

5, 10 und 15 Stunden post inj. erfolgte die Tötung der Tiere durch Dekapitation. Blut (wobei das Kopfblut und das Blut des übrigen Körpers getrennt gewonnen und die Seren abzentrifugiert wurden), Herz, Leber und Gehirn wurden entnommen. Die Präparation der Endo- und Perilymphe

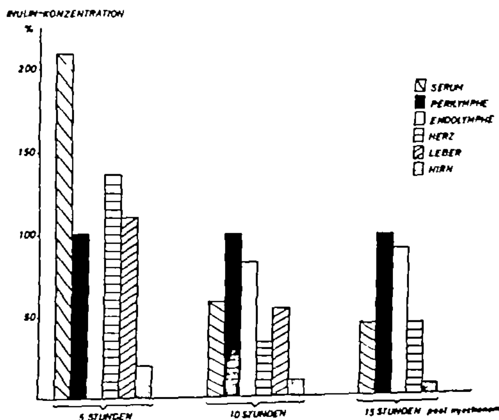


Abb. 10. Vergleich der Inulinkonzentration des Blutserums, der Innenohrflüssigkeiten und Organe. Die Werte beziehen sich auf die Perilymphe, deren Konzentration mit 100 angenommen wurde.

erfolgte auf die übliche bereits beschriebene Weise in der Tiefkühlkammer. Nach Homogenisierung und Aufbereitung des Materials mit Hyaminhydroxyd in einem kochenden Wasserbad und anschließender Zugabe von Diotol erfolgte die Messung in einem Tricarb-Scintillationszähler. Der hier bei entstehende Quentsch Effekt ließ sich anhand einer Eichkurve eliminieren. Die gemessene Impulszahl pro Minute wurde auf das Frischgewicht der Organe bezogen.

Wie Abb. 10 zeigt, gelangt Inulin trotz seines hohen Molekulargewichtes von 6000 offensichtlich ohne Schwierigkeiten in das Innenohr. Das bedeutet, da eine Sekretion ausgeschlossen werden kann, daß der Eintritt in die Innenohrräume entweder durch Filtration oder über eine Diffusion erfolgen muß. Dieser Befund ist für die Physiologie des Innenohres von Interesse, da bis in die jüngste Zeit hinein die Auffassung vorherrschte, daß die Innenohrflüssigkeiten ein Sekretionsprodukt z. B. der Stria vascularis darstellen. Die Inulinversuche sprechen vielmehr für die neuerdings von Schindler wiederaufgegriffene Theorie, wonach zumindest die Perilymphe als ein Ultrafiltrat des Blutes anzusehen ist. In Anbetracht des etwa gleich hohen Inulingehaltes der Endolymphe drängt sich die Frage auf, ob nicht auch für die Endolymphbildung Filtrationsvorgänge oder eine Diffusion aus dem Perilymphraum durch die Reissner'sche Membran verantwortlich sind.

Der Inulinversuch vermittelt nicht nur einen Einblick in die Entstehung der *Innenohrflüssigkeiten*, sondern darüberhinaus auch in ihren Austausch. Die nicht resorbierbaren Stoffe wie Inulin gelangen zwar leicht in die Innenohrräume, aber offensichtlich nur schwer wieder heraus. Verglichen mit anderen gut resorbierbaren Stoffen bleibt Inulin viel länger im *Innenohr* zurück und erreicht hier Konzentrationen, die mehr als das Doppelte des *Blutspiegels* ausmachen. Die *Anreicherung des Inulins* kann wahrscheinlich darauf zurückgeführt werden, daß es aus dem Innenohr nicht aktiv rückresorbiert wird, sondern nur *diffundieren* kann. Demgegenüber scheinen gut resorbierbare Stoffe leichter eliminierbar zu sein, da sie zusätzlich der aktiven Rückresorption durch die *Zellen der Stria vascularis* oder des Ductus endolymphaticus unterliegen. Dieser Ausweg aus dem Innenohr steht dem Inulin nicht zur Verfügung. Das Verhalten des Inulins, das *man auch als Inulinclearance* des Innenohres bezeichnen könnte, zeigt, wie weit ein *Stoffaustausch* im Innenohr allein durch Filtration und *Diffusion und* unabhängig von aktiven Resorptions- und Sekretionsprozessen *möglich* ist.

Die Kumulation der Aminoglykosidantibiotika im Innenohr

Darüberhinaus bringen uns die Inulinbefunde auch einer Erklärung der Kumulationsvorgänge bei den Streptomycesantibiotika näher. Kanamycin z. B. erreicht, wie oben bereits gezeigt wurde, in einer niedrigen Dosierung von 15 oder 25 mg/kg, die praktisch aequimolar ist mit der oben angewandten Inulindosis, einen mit Inulin vergleichbaren Innenohrspiegel. Er beträgt ebenfalls 6 Stunden post inj. das 2,5-fache des Blutspiegels *und*

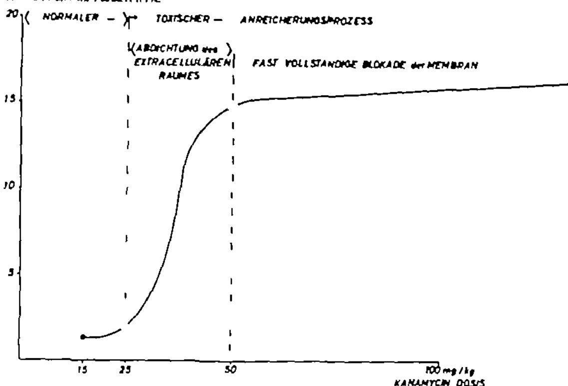


Abb 11 Kanamycinkonzentration in Perilymphe und Kanamycinsulfat Dosis. (Alle Werte bezogen auf Kanamycin Base)

ein vielfaches der Organkonzentration In diesem Dosisbereich weisen die beiden nicht resorbierbaren Substanzen das ungiftige Inulin und die toxischen Aminoglykosidantibiotika in ihrem Verhalten im Innenohr eine weitgehende Übereinstimmung auf In der Anreicherung schwer resorbierbarer giftiger Stoffe im Innenohr ist wahrscheinlich die primäre Ursache für die Ototoxikose zu sehen Sie geht der eigentlichen Innenohrschädigung voraus und könnte als die erste, einleitende Phase der Intoxikation bezeichnet werden (Abb 11)

Mit steigendem Kanamycingehalt wird schließlich eine toxische Schwellenkonzentration erreicht In dem Augenblick wo die Dosis von 25 mg/kg überschritten wird tritt wie Abb 7 zeigt eine entscheidende Änderung im Verhalten des Kanamycins auf Wir haben sie in der Abb 11 als 2 Phase des Intoxikationsverlaufs bezeichnet In diesem Stadium kommt es zu einem sprunghaften Anstieg der Innenohrkonzentration Es besteht der Verdacht daß die verstärkte Retention des Kanamycins bereits Ausdruck einer toxischen Innenohrschädigung ist

Wir neigen zu der Auffassung, daß es sich hier wahrscheinlich um die ersten Zeichen einer gestörten Permeabilität der Innenohrmembranen handelt Diese Vorstellung stützt sich auf experimentelle Befunde und Untersuchungen die z. Zt noch weiter fortgesetzt werden aber bereits folgen des erkennen lassen Es zeigte sich daß der Transport markierter Kalium Ionen die in den Perilymphraum die Scala vestibuli oder Scala tympani eingebracht worden waren und normalerweise sehr schnell durch die Reiss-

ner sche Membran in die Endolymphe übertreten und dann von der Stria vascularis des Endolymphraumes aufgenommen werden, durch Kanamycin weitgehend zum Erliegen kommt. Kanamycin übertrifft in dieser permeabilitätshemmenden Eigenschaft sogar alle anderen bekannten Membrangifte wie Strophanthin G, Monojodessigsäure oder Salyrgan, deren Wirkung auf das Innenohr wir bereits früher untersuchten. Bemerkenswert ist, daß die ersten Zeichen einer herabgesetzten Durchlässigkeit der Membran in dem offenbar kritischen Dosisbereich über 25 mg/kg Kanamycin zu beobachten sind, also gerade in dem Augenblick, wo auch der steile Anstieg des Kanamycinspiegels im Innenohr erfolgt. Man kann hieraus auf einen ursächlichen Zusammenhang schließen. Die Annahme liegt nahe, daß die verminderte Membranpermeabilität für Kalium wahrscheinlich auch für die Anhäufung des Kanamycins verantwortlich ist.

Ebenso läßt sich auch die 3. Phase der Intoxikation, die durch den flachen Verlauf der Sättigungskurve, d. h., mit anderen Worten durch ein Sistieren des Anreicherungsprozesses (Abb. 7 bzw. 11) charakterisiert wird, als einen Membraneffekt deuten. Sie könnte durch eine nunmehr vollständige Abdichtung der Innenohrmembranen nicht nur für Kanamycin, sondern auch für andere gut resorbierbare Stoffe wie z. B. für Ionen erklärt werden. Damit käme auch der Wassertransport im Innenohr zum Erliegen. Die Folge ist wahrscheinlich ein Stillstand der gesamten Lymphzirkulation und des Lymphaustausches im Innenohr, so daß keine neue kanamycinhaltige Lymphe mehr in das Innenohr gelangt und der Anreicherungsvorgang zum Erliegen kommen muß.

Die verschiedenen Phasen des Intoxikationsprozesses könnte man sich folgendermaßen vorstellen. Als erstes morphologisches Substrat der Intoxikation werden von allen Untersuchern übereinstimmend Zellvergrößerungen und Kernschwellungen beschrieben. Diese Veränderungen betreffen nicht nur die Haarzellen, sondern auch die Stützzellen und Epithelien der Stria vascularis, also praktisch alle Zellen des Innenohres mehr oder weniger stark je nach ihrer Empfindlichkeit. Denkbar wäre, daß hierdurch zunächst nur eine Abdichtung der Innenohrmembranen, d. h., genauer gesagt ihrer interzellulären Spalten hervorgerufen wird, jenes Raumes also, der gerade für den Transport der überwiegend extrazellulären Substanzen wie Streptomycin von entscheidender Bedeutung ist. Auf diese Weise wird die Ausscheidung der toxischen Antibiotika gehemmt und ihre Anhäufung im Innenohr gefördert. Kanamycin würde sich also in diesem Falle selbst, infolge einer toxischen Membranwirkung, den Ausweg aus dem Innenohr blockieren und wäre damit für seine vermehrte Anreicherung ursächlich verantwortlich. Die 2. Phase der Anreicherung ließe sich durch eine derartige erschwerte Diffusion zwanglos erklären. Erst in der 3. Phase scheint es dann mit dem Erlöschen der Zellfunktion zu einem Sistieren auch der aktiven Resorptionsvorgänge in den Zellen zu kommen, wodurch der Ionen- und Flüssigkeitsaustausch behindert wird und schließlich zum Erliegen kommt.

Der charakteristische Verlauf der Kanamycinanreicherung im Innenohr könnte auch noch auf andere Weise gedeutet werden. Denkbar wäre z. B. eine Schranke zwischen Blut und Innenohrlymphe, die erst bei einer bestimmten Kanamycinkonzentration im Blut überschritten werden kann. Gegen diese Hypothese ist jedoch einzuwenden, daß unterhalb der angenommenen Schwellenkonzentration bereits relativ große Kanamycinmengen in das Innenohr gelangen.

Als weitere Ursache für die Anhäufung wäre im Innenohr auch eine chemische Bindung des Kanamycins, z. B. an saure Substanzen der Innenohrlymphe vorstellbar. Die Sättigung könnte in diesem Falle als ein Erschöpfen der zur Verfügung stehenden Bindungskapazität aufgefaßt werden. Zur Klärung dieser Frage sind weitere Untersuchungen vor allem mit Hilfe der Dünnschichtchromatographie vorgesehen, die zeigen sollen, ob eine evtl. Kopplung des Kanamycins an Substanzen der Innenohrflüssigkeiten vorliegt. Gegen diese Annahme allerdings spricht, daß in anderen extrazellulären Flüssigkeiten eine solche Bindung nicht zu beobachten ist.

VII. Vergleich der Kanamycin-, Streptomycin-, Dihydrostreptomycin- und Neomycinspiegel im Organismus

Die übrigen Antibiotika der Oligosaccharidgruppe Streptomycin, Dihydrostreptomycin und Neomycin unterscheiden sich hinsichtlich ihres Verhaltens im Organismus grundsätzlich nicht vom Kanamycin. Sie werden *ebenfalls im Innenohr angereichert und nur sehr langsam wieder ausge-*

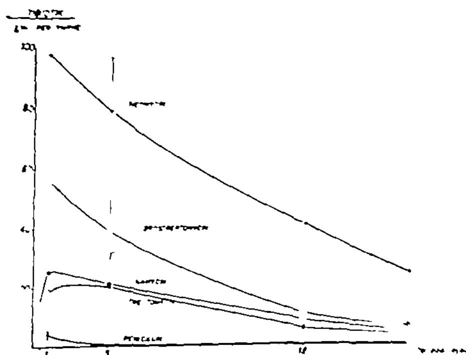


Abb. 1. Antibiotikaspiegel in der Perilymphe bei gleicher Dosierung [illegible] mg/kg (außer Neomycin, von dem hier lediglich 100 mg/kg verabreicht wurden)

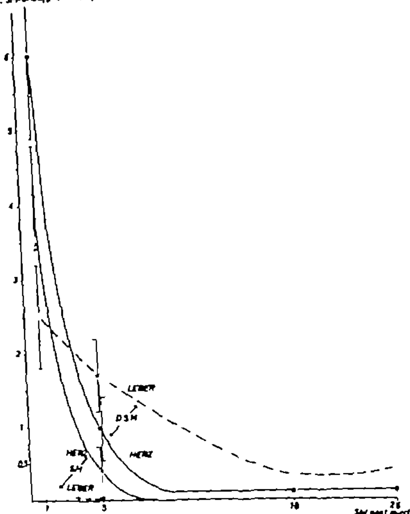


Abb. 13 Streptomycin (SM) und Dihydrostreptomycin (DSM)-Gehalt i. Leber und Herz bei gleicher Dosis.

schieden. Dennoch weisen sie einige bemerkenswerte Unterschiede auf, die eine genauere Betrachtung wert sind.

Auf Abb. 12 sind zum Vergleich die Perilymphspiegel der verschiedenen Streptomycesantibiotika dargestellt. Streptomycin weist hier verglichen mit den anderen Antibiotika dieser Gruppe bei gleicher Dosierung den niedrigsten Innenohrspiegel auf. Nur wenig höher verläuft die Konzentrationskurve des Kanamycins. Die geringe Differenz zwischen Kanamycin und Streptomycin ist nicht signifikant.

Auch der Blutspiegel des Dihydrostreptomycins entsprach weitgehend dem des Streptomycins. Dagegen fiel eine wesentlich höhere Konzentra-

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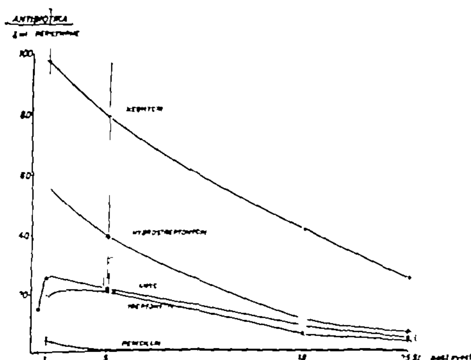


Abb. 1. Antibiotikaspiegel in der Perilymphe bei gleicher Dosierung von 250 mg/kg, außer Neomycin, von dem hier lediglich 100 mg/kg verabreicht wurden.

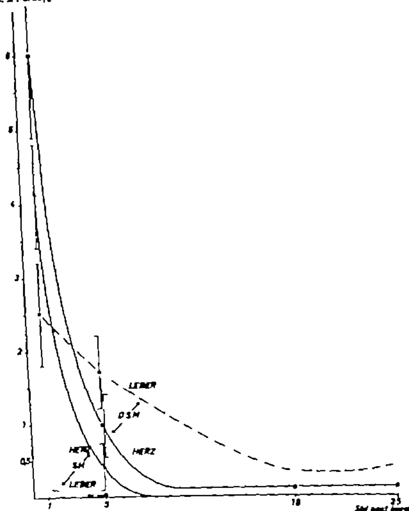


Abb 13 Streptomycin (SM) und Dihydrostreptomycin (DSM)-Gehalt i Leber und Herz bei gleicher Dosis.

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tion des Dihydrostreptomycins sowohl im Innenohr als auch im Herz und in der Leber auf (Abb 13)

Die höheren Organ und Innenohrspiegel des Dihydrostreptomycins lassen sich gegenüber *Kanamycin und Streptomycin statistisch sichern* ($p < 0\,005$) Aus diesen Befunden könnte man den Schluß ziehen, daß Dihydrostreptomycin nicht, wie vielfach angenommen wird ototoxischer ist als Streptomycin, *sondern seine stärkere ototoxische Wirkung lediglich* seiner höheren Konzentration am Schadigungsort verdankt So findet auch die Tatsache, daß Dihydrostreptomycin trotz seiner geringeren akuten bzw Allgemeintoxizitat stärkere Innenohrschädigungen verursacht als Streptomycin eine Erklärung. Die Diskussion über diese umstrittenen und für die therapeutische Anwendung entscheidenden Vor und Nachteile des DSM ging über viele Jahre hin und führte schließlich zum Verbot des Dihydrostreptomycins. — Es muß jedoch hinzugefügt werden, daß ein höherer Dihydrostreptomycinspiegel bisher nur im Innenohr des Meerschweinchens aber noch nicht beim Menschen nachgewiesen werden konnte. Zwar soll nach Müsebeck DSM beim Meerschweinchen genauso wie beim Menschen stärkere Hörschädigungen hervorrufen als SM Jedoch gehen hierüber die Ansichten der einzelnen Untersucher sehr auseinander so daß eine endgültige Beurteilung z. Zt noch nicht möglich ist

Sicherlich würde es zu weit führen, wollte man die unterschiedliche Toxizität der einzelnen Antibiotika der Aminoglykosidgruppe ausschließlich von ihrer Konzentration im Innenohr her erklären. Das würde letzlich bedeuten, daß sämtliche Stoffe, die gleiche Toxizität besitzen was aber kaum anzunehmen ist Soviel darf aber heute auf Grund dieser Befunde schon gesagt werden daß der Konzentration eine größere Bedeutung *zuzukommen scheint als man bisher vermutete*

Allgemein wird heute zumindest beim Menschen das Streptomycin als das am wenigsten ototoxische Antibiotikum der Aminoglykosidgruppe angesehen Danach folgt das Dihydrostreptomycin Kanamycin und Neomycin Vergleicht man diese Reihenfolge mit der Folge ihrer Konzentrationen im Innenohr wie sie auf Abb 12 dargestellt sind nämlich Streptomycin, Kanamycin Dihydrostreptomycin und Neomycin, so fällt zwar eine große Ähnlichkeit auf aber es besteht keine vollständige Übereinstimmung So spricht vor allem gegen die bisherigen Vorstellungen die Tatsache daß Kanamycin obwohl es stärker toxisch ist im Innenohr in einer geringeren Konzentration vorkommt als Dihydrostreptomycin Von dieser Ausnahme abgesehen scheinen aber die Befunde besonders deutlich kommt dies am Beispiel des Neomycins zum Ausdruck auf eine Beziehung zwischen der Innenohrkonzentration der Antibiotika und ihrer Ototoxizität hinzuweisen

Neomycin mußte im Rahmen dieser vergleichenden Untersuchungen infolge seiner wesentlich stärkeren toxischen Wirkung in viel niedrigerer Dosierung angewandt werden als Kanamycin SM und DSM Obwohl am Anfang nur 100 mg Neomycin/kg verabreicht wurden war der Innenohrspiegel 4 mal so hoch wie bei einer 2 ½-fach höheren Kanamycindosis

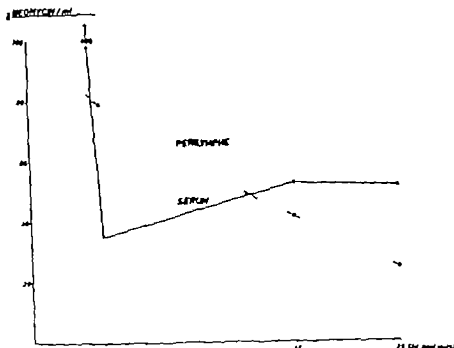


Abb. 14 Neomycinspiegel im Blutserum und in der Perilymphe nach einmaliger Injektion einer hohen nephrotoxischen Dosis (100 mg/kg)

Es liegt nahe die viel stärkere Ototoxizität des Neomycins auf die besonders ausgeprägte Kumulationsneigung dieser Substanz im Innenohr zurückzuführen. Diese Schlußfolgerung scheint aber hier nicht zuzutreffen.

Bei einer genaueren Betrachtung fällt auf daß der Blutspiegel des Neomycins nicht nur viel höher ist, sonder auch außergewöhnlich lange bestehen bleibt (Abb 14)

25 Stunden post inj war im Blutserum noch 1/8 der Anfangskonzentration vorhanden, während sich zur gleichen Zeit z. B. von Kanamycin oder Dihydrostreptomycin nur noch 1/2000 nachweisen ließ. Der extrem hohe und lang anhaltende Blutspiegel des Neomycins beruht sehr wahrscheinlich auf einer renalen Ausscheidungsstörung infolge einer toxischen Nierenschädigung. Aus der Literatur ist bekannt, daß bereits nach einer einmaligen Gabe von 100 mg Neomycin beim Meerschweinchen schwere Nierenschädigungen auftreten. Die hohe Neomycinkonzentration in den Innenohrflüssigkeiten muß in diesem Fall auf den extrem hohen Blutserumspiegel zurückgeführt werden und kann noch nicht als Ausdruck einer spezifischen Kumulationsneigung des Neomycins aufgefaßt werden. Dieser Befund bestätigt aber die aus zahlreichen Untersuchungen und klinischen Beobachtungen bekannte erheblich stärkere Ototoxizität des Neomycins, die jedoch hier wie in zahlreichen klinischen Fällen nur eine Folge der besonders ausgeprägten nephrotoxischen Wirkung darstellt.

TABELLE 2. *Neomycinkonzentration nach subkutaner Injektion von 25 mg Neomycinsulfat/kg Meerschweinchen*

Std. post. inj.	Perilymphe	Serum	Herz	Leber	Gehirn
1	111 (±69)	29 (±13)	Spur (<0,1)	—	—
5	45 (±21)	3,5 (±4,7)	—	—	—
18	20 (±6,6)	<0,1	—	—	—
25	10,6 (±3,7)	<0,1	—	—	—

γ Neomycin/ml (g Trockengewicht)

Um sich ein klareres Bild über die ototoxische Eigenschaft des Neomycins machen zu können, mußte der Einfluß einer Nierenschädigung ausgeschlossen werden. Hierzu war es notwendig, die Neomycindosis noch weiter bis auf 25 mg/kg, d. h., 1/10 der sonst bei den Streptomycinantibiotika üblichen Dosis, zu reduzieren. Bei dieser Dosierung lassen sich Neomycinblutspiegel erzielen, die praktisch denen einer gleich hohen Kanamycininjektion entsprechen. Eine verzögerte Ausscheidung als Zeichen einer renalen Intoxikation war jetzt nicht mehr zu beobachten. Trotzdem erreichte die Neomycinkonzentration in der Perilymphe noch eine überraschende Höhe, wie wir sie bisher bei keinem anderen Antibiotikum gesehen haben. Sie betrug gut das 5-fache der Innenohrkonzentration, die sonst bei einer 10-fach höheren Dosierung mit Kanamycin erreicht wird und übertraf sogar den maximalen Neomycin-Blutspiegel um mehr als das 3fache (Tab. 2). In den übrigen Organen fand sich dagegen überhaupt kein Neomycin, bzw. die Neomycinkonzentration lag unter der Nachweisgrenze von 0,1 γ/g.

Für diese ausgeprägte Kumulation und Retention des Neomycins in der Perilymphe haben wir keine andere Erklärung als die Annahme einer substanzspezifischen Kumulationsneigung, deren Ursache möglicherweise auf einer membranblockierenden Wirkung beruht, wie wir sie bereits bei Kanamycin diskutiert haben. Es liegt nahe, die stärkere haarzellschädigende Wirkung des Neomycins *ausschließlich als einen Konzentrationseffekt* zu deuten. Jedoch scheinen die Verhältnisse, wie die Wechselwirkungen zwischen der Konzentration einerseits und der toxischen Schädigung auf der anderen Seite zeigten, in Wirklichkeit komplizierter zu sein. Die hohe Konzentration bedingt zwar primär die Schädigung des Innenohres, umgekehrt begünstigt aber die Schädigung wiederum eine verstärkte Anreicherung, so daß eine genaue Feststellung von Ursache und Folge kaum möglich ist.

VIII. Untersuchungen zur Frage der Toxizitätsminderung

1. *Das Verhalten der verschiedenen Pantothenatverbindungen des Kanamycins im Vergleich mit dem Sulfatsal*

In Anbetracht der engen Beziehungen, die zwischen der Ototoxizität und der Konzentration der Streptomycesantibiotika im Innenohr zu bestehen

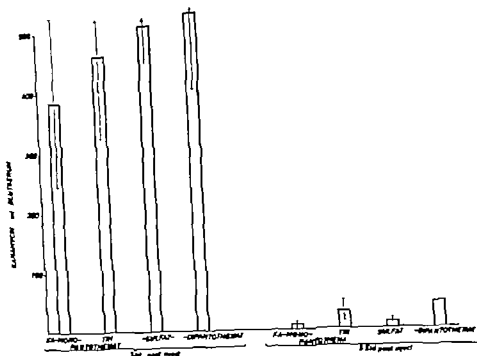


Abb. 15. Blutspiegel verschiedener Kanamycinverbindungen. (Alle Werte sind auf die Kanamycinbase bezogen.)

scheinen, mußte man sich fragen, ob nicht die geringere Toxizität, die vor allem den Pantothenatsalzen der Streptomycesantibiotika nachgesagt wird, möglicherweise auf einer niedrigeren Konzentration dieser Substanzen in den Innenohrflüssigkeiten beruht. Es wurden die Spiegel verschiedener Pantothenatverbindungen, des Kanamycin-Monopantothenats, des Kanamycindipantothenats und des Kanamycintripantothenats sowie des Kanamycinsulfates untersucht. Um vergleichbare, aequimolare Kanamycinmengen zu erhalten, war es wegen der unterschiedlichen Molekulargewichte dieser Substanzen erforderlich, die Dosis jeweils auf die Kanamycinbase zu beziehen.

Bereits eine Stunde nach der Injektion konnte man feststellen, daß sich das Monopantothenat gegenüber den Di- und Tripantothenatverbindungen durch einen etwas niedrigeren Blutspiegel auszeichnet. Dieser Befund ließ sich allerdings statistisch infolge der geringen Versuchszahl noch nicht sichern (Abb. 15).

Durch die deutlich langsamere Ausscheidung der Di- und Tripantothenate verglichen mit dem Monopantothenat vergrößerte sich die Differenz im weiteren Verlauf des Versuches. 5 Stunden post inj., als der Blutspiegel des Monopantothenates wieder auf 2% gesunken war, der Blutspiegel der Di- und Tripantothenate aber immerhin mit 6–8% noch gut 3 mal so hoch war wie der des Monopantothenates, ließ sich der Unterschied mit $p < 0{,}01$ statistisch sichern.

Tabelle 2. *Neomycinkonzentration nach subkutaner Injektion von 25 mg Neomycinsulfat/kg Meerschweinchen*

Std. post. inj.	Perilymphe	Serum	Herz	Leber	Gehirn
1	111 (±69)	29 (±13)	Spur (<0,1)	—	—
5	45 (±21)	3,5 (±4,7)	—	—	—
18	20 (±6,0)	<0,1	—	—	—
25	10,6 (±3,7)	<0,1	—	—	—

γ Neomycin/ml (g Trockengewicht)

Um sich ein klareres Bild über die ototoxische Eigenschaft des Neomycins machen zu können, mußte der Einfluß einer Nierenschädigung ausgeschlossen werden. Hierzu war es notwendig, die Neomycindosis noch weiter bis auf 25 mg/kg, d. h., 1/10 der sonst bei den Streptomycinantibiotika üblichen Dosis, zu reduzieren. Bei dieser Dosierung lassen sich Neomycinblutspiegel erzielen, die praktisch denen einer gleich hohen Kanamycininjektion entsprechen. Eine verzögerte Ausscheidung als Zeichen einer renalen Intoxikation war jetzt nicht mehr zu beobachten. Trotzdem erreichte die Neomycinkonzentration in der Perilymphe noch eine überraschende Höhe, wie wir sie bisher bei keinem anderen Antibiotikum gesehen haben. Sie betrug gut das 5-fache der Innenohrkonzentration, die sonst bei einer 10-fach höheren Dosierung mit Kanamycin erreicht wird und übertraf sogar den maximalen Neomycin-Blutspiegel um mehr als das 3-fache (Tab. 2). In den übrigen Organen fand sich dagegen überhaupt kein Neomycin, bzw. die Neomycinkonzentration lag unter der Nachweisgrenze von 0,1 γ/g.

Für diese ausgeprägte Kumulation und Retention des Neomycins in der Perilymphe haben wir keine andere Erklärung als die Annahme einer substanzspezifischen Kumulationsneigung, deren Ursache möglicherweise auf einer mebranblockierenden Wirkung beruht, wie wir sie bereits bei Kanamycin diskutiert haben. Es liegt nahe, die stärkere haarzellschädigende Wirkung des Neomycins ausschließlich als einen Konzentrationseffekt zu deuten. Jedoch scheinen die Verhältnisse wie die Wechselwirkungen zwischen der Konzentration einerseits und der toxischen Schädigung auf der anderen Seite zeigten, in Wirklichkeit komplizierter zu sein. Die hohe Konzentration bedingt zwar primär die Schädigung des Innenohres, umgekehrt begünstigt aber die Schädigung wiederum eine verstärkte Anreicherung, so daß eine genaue Feststellung von Ursache und Folge kaum möglich ist.

VIII. Untersuchungen zur Frage der Toxizitätsminderung

1. *Das Verhalten der verschiedenen Pantothenatverbindungen des Kanamycins im Vergleich mit dem Sulfatsal*

In Anbetracht der engen Beziehungen, die zwischen der Ototoxizität und der Konzentration der Streptomycesantibiotika im Innenohr zu bestehen

namycinsalze an der Abnahme der Mikrophonpotentiale und fand ebenfalls unter Kanamycinmonopantothenat keine Schädigung des Gehörs, während die Di- und Tripantothenate einen ähnlichen Hörabfall hervorriefen wie Kanamycinsulfat. Er teilte uns kürzlich mit, daß er unserer Ansicht zu stimmt und ebenfalls die Ursache für die verschieden starke Toxizität als eine Konzentrationsfrage auffaßt.

Größere Schwierigkeiten bereitet jedoch ein Vergleich der Pantothenat gruppe mit dem Sulfatsalz. Die Blutkonzentrationen der Kanamycin-Pantothenate und des Kanamycinsulfates wiesen zwar 1 Stunde nach der Injektion Unterschiede auf, die insofern Beachtung verdienen, da sie eine überraschende Übereinstimmung mit den Ergebnissen Tybergheins erkennen ließen (Abb 15) Es zeigt sich, daß die Substanzen mit der größten Toxizität wie die Sulfat und Dipantothenatverbindungen auch den höchsten Blutspiegel erreichten, gefolgt von dem etwas weniger giftigen Tripantothenat, während kanamycinmonopantothenat den eindeutig niedrigsten Blutspiegel aufwies. Die Reihenfolge ihrer Konzentration würde also genau ihrer toxischen Wirksamkeit entsprechen. So interessant diese Feststellung auch sein mag, so muß doch zu Bedenken gegeben werden, daß die relativ geringen Konzentrationsunterschiede in Anbetracht der großen Streuung und zu niedrigen Versuchszahl statistisch noch nicht zu sichern waren.

Für Möckter und Mitarbeiter waren diese Befunde von besonderem Interesse, da sie der entgiftenden Wirkung der Pantothenate große praktische Bedeutung beimessen. Sie reproduzierten die gleichen Versuche daraufhin nochmals an Meerschweinchen und Ratten. Dabei ergaben sich ebenfalls eine Stunde post inj für Kanamycinsulfat die Höchsten Blutkonzentrationen, während die Pantothenatsalze bis zu 15% niedriger lagen. Eine statistisch signifikante Differenz gegenüber Kanamycinsulfat konnte allerdings hier nur für Kanamycintripantothenat ermittelt werden.

2 bzw 5 Stunden nach einer Injektion war der Blutspiegel, wie auch Möckter und Mitarbeiter übereinstimmend mit unseren Versuchen zeigen konnten, vor allem für Kanamycinsulfat, das offensichtlich schneller als die größeren Pantothenatmoleküle eliminiert wird, bereits erheblich gesunken. Der unterschiedliche Konzentrationszeitverlauf des Sulfates im Vergleich zu den Pantothenaten führt im weiteren Verlauf zu einer Änderung und Umkehr des Sulfat Pantothenatverhältnisses.

Für das Innenohr läßt sich anhand der Konzentrationskurven auf Abb. 16 sagen, daß bei gleich hoher aequimolarer Dosierung die Di- und Tripantothenatverbindungen einen höheren Spiegel aufweisen als das Kanamycinsulf tsalz, während die Konzentration des Kanamycinmonopantothenates der des Kanamycinsulfates weitgehend entspricht. Wenn man unterstellt, daß Kanamycin Di- und Tripantothenat trotz höherer Innenohrkonzentration angeblich nicht toxischer sein soll, könnte man hieraus auf eine, wenn auch nur relative Schutzwirkung der Pantothensäure, schließen. Dieser Effekt tritt allerdings bei gleicher Dosierung nicht in Erscheinung, da

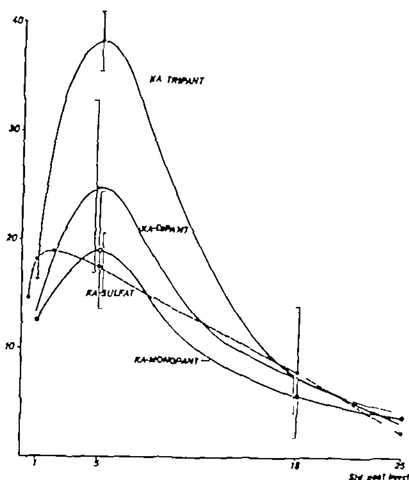
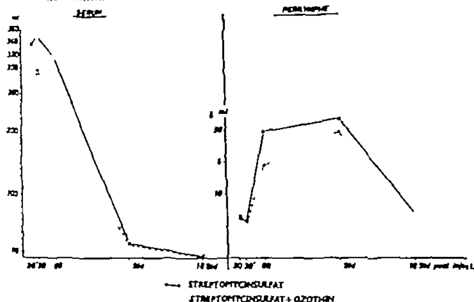


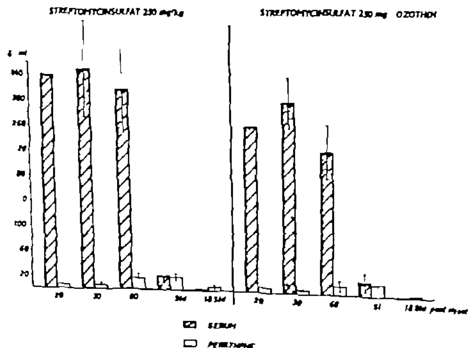
Abb 16 Perilymphspiegel verschiedener Kanamycinsal e (Alle Werte be iehe ich auf die Kanamycin Base)

Ähnlich wie im Blut verhielten sich die Kanamycinpantothenate auch in den Innenohrflüssigkeiten (Abb 16)

In den ersten Stunden nach der Injektion ließen die Innenohrkonzentrationen der verschiedenen Substanzen zunächst nur geringe Unterschiede erkennen Im weiteren Verlauf wurden die Differenzen immer deutlicher 5 Stunden nach der Injektion zeigte es sich auch hier daß Kanamycinmonopantothenat von allen Pantothenaten die weitaus geringste Konzentration aufweist Der Gehalt der Innenohrflüssigkeiten an Kanamycinmonopantothenat war mit 19 γ/ml Perilymphe signifikant niedriger ($p < 0\ 01$) als an Tripantothenat mit 38 γ/ml Der Unterschied zum Dipantothenat mit 25 γ/ml ließ sich nicht sichern ($p < 0\ 1$) Zwischen dem Verhalten der Kanamycinpantothenate im Blut und in den Innenohrflüssigkeiten scheint eine Beziehung zu bestehen Wahrscheinlich ist die niedrigere Blutkonzentration des Monopantothenates für die geringere Innenohrkonzentration und somit für die schwächere ototoxische Wirkung dieser Verbindung ursächlich verantwortlich zu machen

Tybergheln bestimmte die unterschiedliche Toxizität der einzelnen Ka





b

Abb. 17 b. Vergleich der Streptomycinspiegel mit und ohne Ozothin.

er durch die höhere Konzentration der Pantothenatverbindungen im Innenohr wieder aufgehoben wird

Die Perilymphspiegel der Kanamycinpantothenatverbindungen weisen zwar für sich betrachtet eine gute Relation zu den Toxizitätsuntersuchungen Tybergheins auf Sie sind nicht nur eine weitere Bestätigung, sondern geben uns auch eine Erklärung dafür warum offensichtlich Kanamycinmonopantothenat von allen Kanamycinpantothenatverbindungen die geringste Toxizität besitzt Kanamycinmonopantothenat ist genau gesagt, nicht weniger ototoxisch als die Tri und Dipantothenatverbindungen, sondern kommt nur in einer geringen Konzentration im Innenohr vor

Nicht hiermit in Einklang zu bringen ist jedoch der ebenfalls relativ niedrige dem Kanamycinmonopantothenat entsprechende Innenohrspiegel des Kanamycinsulfats Sowohl Tybergheln als auch J P Brun (mündliche Mitteilung) sahen bei elektrophysiologischen und histologischen Untersuchungen eine signifikant geringere Toxizität des Kanamycinmonopantothenats im Vergleich zum Sulfatsalz. Dagegen kamen kürzlich Merkle Plattig und Keidel (1968) aufgrund elektrophysiologischer und histologischer Untersuchungen an der Katze zu dem Schluß daß Kanamycinpantothenat genauso toxisch ist wie Kanamycinsulfat während sich die Kanamycin Di und Tripantothenate als stärker toxisch erwiesen Diese letzteren Ergebnisse zeigen interessanterweise genau eine Parallele zu den Konzentrationsverhältnissen dieser Kanamycinverbindungen im Innenohr wie sie Abb 16 darstellt

Eine Erklärung für die zum Teil abweichenden Befunde der verschiedenen Untersucher ist darin zu sehen, daß die Schutzwirkung bzw die Toleranzverbesserung durch Pantothensäure nach Schätzung Müsebecks im günstigsten Fall 30% ausmacht Vielleicht ist gerade in diesem relativ geringen, und darum auch verständlicherweise nur schwer zu sichernden Toxizitätsunterschied zwischen der Sulfat und Pantothenatverbindung die Ursache zu suchen, warum die Schutzwirkung der Pantothensäure nur von einigen Untersuchern beobachtet, von anderen aber nicht festgestellt werden konnte und abgelehnt wird Man möchte hier der Ansicht Müsebecks zustimmen, daß die Ursache für die unterschiedlichen Ergebnisse im Tierexperiment in der bewusst zur Erzielung schwerer toxischer Schädigungen angewandten, viel höheren Dosierung zu suchen ist so dass die geringe toxizitätsmindernde Wirkung der Pantothenate überlagert wird und nicht mehr in Erscheinung tritt

2 Hat Ozothin einen Einfluss auf die Streptomycesantibiotika?

In jüngster Zeit wurde durch zahlreiche Publikationen der Freiburger Hals- Nasen u Ohrenklinik das Interesse vor allem auf Ozothin (s. Seite 48) gelenkt, daß u a als Losungsmittel für Antibiotika Anwendung findet Holz und Mitarbeiter machten die Beobachtung daß Ozothin die toxische Wirkung nicht nur des Streptomycins, sondern auch der übrigen Aminoglykosidantibiotika, praktisch vollständig verhindern soll Dieser Ef

TABELLE 3. *Streptomycinkonzentration in γ/g 1 bzw. 5 Stunden nach subkutaner Injektion von 250 mg Streptomycin/kg Meerschweinchen und 250 mg in Ozothin gelöstem Streptomycin/kg*

		Herz		Leber		Gehirn	
1 Std. post Inj.	Streptomycin	5,3	±0,3	0,39	±0,27	0,52	±0,23
	Streptomycin + Ozothin	1,3	±0,5	0,16	±0,03	0,17	±0,057
5 Std. post Inj.	Streptomycin	0,3	±0,07	0,013	±0,012	0,023	±0,012
	Streptomycin + Ozothin	0,04	±0,011	0		0	

keine cochleotoxischen Schäden mehr fanden. Dagegen vermag Ozothin unter den gleichen Versuchsbedingungen, wie Lange, der der Arbeitsgruppe um Holz angehört, unlängst berichtete, die im Allgemeinen wesentlich stärkeren vestibulären Störungen und morphologisch nachweisbare Schäden am peripheren Gleichgewichtsapparat nicht zu verhindern. Es zeigte sich kein Unterschied im Vergleich zu den Tieren, die nur SM erhalten hatten.

Dieser Befund überrascht nicht weiter, sondern bestätigt vielmehr den Verdacht, daß die Ozothinwirkung auf einer Herabsetzung der Streptomycinkonzentration beruht. Da die toxische Schwelle für das Hörorgan bei Streptomycin bekanntlich wesentlich höher liegt als die des Gleichgewichtsapparates, genügt wahrscheinlich die durch Ozothin hervorgerufene Konzentrationsminderung, um Hörschäden zu vermeiden. Sie reicht aber offensichtlich nicht aus, um auch Gleichgewichtsstörungen zu verhüten. Die niedrigere toxische Schwelle für das Gleichgewichtsorgan erfordert, wenn man vestibuläre Schäden ausschließen will, eine noch stärkere Herabsetzung des Streptomycinspiegels. Hierzu genügt Ozothin allein offenbar nicht.

Die Tatsache, dass Ozothin bei etwas stärker wirkenden Substanzen, wie z. B. Kanamycin, ebenfalls keinen Schutzeffekt mehr besitzt, könnte auf die gleiche Weise erklärt werden. Tyberghein kam nach eingehenden Untersuchungen zu der Feststellung, dass Ozothin nicht in der Lage ist, die Abnahme der Mikrophonpotentiale zu verhindern. Er glaubt sogar unter Ozothin eher stärkere Schädigungen gesehen zu haben.

Zu dem gleichen Ergebnis gelangte kürzlich auch J. P. Brun, der bei quantitativen, histologischen Untersuchungen an Cytocochleogrammen unter Kanamycinsulfat, ohne und mit Ozothin, die gleichen Haarzellschädigungen sah.

Trotz dieser negativen Beurteilungen des Ozothins kann man, im Hinblick auf die nachgewiesen Konzentrationsverminderung der toxischen Antibiotika sagen, Ozothin vermag, zwar in geringem Umfang, ototoxische Schäden zu verhüten.

Es i t aber nicht in der Lage, Streptomycin zu entgiften. Eine Entgiftung

fekt soll auch dann noch eintreten, wenn Ozothin und das Antibiotikum nicht in einer gemeinsamen Lösung injiziert, sondern getrennt verabreicht werden Erstaunlicherweise tritt die Schutzwirkung des Ozothins angeblich nur dann ein, wenn Ozothin gleichzeitig oder vorher mit dem Antibiotikum verabfolgt wird Sie *bleibt dagegen aus, wenn Ozothin erst eine oder wenige* Minuten später injiziert wird Da dieser günstige Ozothineffekt nur von Holz und Mitarbeitern bisher beschrieben wurde von allen anderen Untersuchern aber nicht bestätigt werden konnte erschienen weitere Untersuchungen angebracht Hier geht es vor allem darum zu klären worauf diese angeblich toxizitätsmindernde Eigenschaft des Ozothins beruht Die Frage die man sich auch hier zuerst stellen muss, lautet Ist die Ozothinwirkung lediglich auf einen *Konzentrationseffekt* zurückzuführen, oder handelt es sich um eine echte Entgiftung?

Betrachten wir zunächst den Konzentrationszeitverlauf des Streptomycins ohne und mit Ozothin im Blutserum und in den Innenohrflüssigkeiten wie ihn *Cada, Brun und Stupp* bei ihren *Untersuchungen am* Meerschweinchen fanden Abb 17 *a* und *b* zeigt die Blut und Perilymphspiegel des Streptomycins und im Vergleich *dazu* die um 20–25% *niedrigeren Spiegel* bei Ozothinzusatz.

Wie schon bei den Pantothenatverbindungen so fällt auch hier auf daß die Verhältnisse im Blut und in den Innenohrflüssigkeiten sehr ähnlich sind. Man könnte hieraus auf eine Beziehung zwischen der Blut und Innenohrkonzentration schließen

Zu dem gleichen Ergebnis kamen auch Mückler und Mitarbeiter Sie konnten ebenfalls unter Ozothin eine signifikante Herabsetzung des Blutspiegels feststellen Während Ratten normalerweise 1 Stunde nach der Injektion von Streptomycin einen Blutserumspiegel von durchschnittlich 643 μg Streptomycin/ml aufwiesen, lag dieser Wert unter Ozothin bei 354 μg/ml, also um annähernd 50% niedriger Dieser Effekt war wie sich auch bei den Untersuchungen Mücklers zeigte bei Meerschweinchen mit ungefähr 20% nicht so ausgeprägt ließ sich aber noch statistisch sichern Hoffmann und Holz teilten erst kürzlich mit daß auch sie unter Ozothin eine Verminderung des *Blutspiegels feststellen mußten*

Am auffälligsten zeigt sich der Einfluß des Ozothins an den Organen die, wie *ein Vergleich der Gewebsspiegel ergibt* viel weniger Streptomycin aufnehmen als bei den ausschließlich mit Streptomycin behandelten Tieren Wie aus der Tabelle 3 zu ersehen ist vermindert Ozothin den Streptomycingehalt in der Leber um mehr als 50 im Herz und Gehirn sogar um über 70% 5 Stunden post inj war in den Organen der Ozothintiere praktisch kein Streptomycin mehr nachweisbar

Um sich einen genaueren Aufschluß über den Ozothineffekt zu verschaffen müßten zunächst einmal vergleichbare Bedingungen d h gleiche Konzentrationsverhältnisse im Blut und Gewebe bei den Ozothin und Kontrolltieren hergestellt werden In Anbetracht des niedrigeren Streptomycingehaltes unter Ozothin ist es nicht verwunderlich wenn Holz und Mitarbeiter

TABELLE 3 *Streptomycinkonzentration in γ/g 1 bzw. 5 Stunden nach subkutaner Injektion von 250 mg Streptomycin/kg Meerschweinchen und 250 mg in Ozothin gelöstem Streptomycin/kg*

		Herz		Leber		Gehirn	
1 Std. post inj.	Streptomycin	5,3	±0,3	0,39	±0,27	0,62	±0,23
	Streptomycin + Ozothin	1,3	±0,5	0,18	±0,03	0,17	±0,057
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	Streptomycin + Ozothin	0,04	±0,011	0		0	

keine cochleotoxischen Schäden mehr fanden. Dagegen vermag Ozothin unter den gleichen Versuchsbedingungen, wie Lange, der der Arbeitsgruppe um Holz angeh rt, unlängst berichtete die im Allgemeinen wesentlich stärkeren vestibulären Störungen und morphologisch nachweisbare Schäden am peripheren Gleichgewichtsapparat nicht zu verhindern Es zeigte sich kein Unterschied im Vergleich zu den Tieren, die nur SM erhalten hatten.

Dieser Befund überrascht nicht weiter sondern bestätigt vielmehr den Verdacht, daß die Ozothinwirkung auf einer Herabsetzung der Streptomycinkonzentration beruht. Da die toxische Schwelle für das Hörorgan bei Streptomycin bekanntlich wesentlich höher liegt als die des Gleichgewichtsapparates, genügt wahrscheinlich die durch Ozothin hervorgerufene Konzentrationsminderung um Hörschäden zu vermeiden. Sie reicht aber offensichtlich nicht aus, um auch Gleichgewichtsstörungen *zu verhüten. Die* niedrigere toxische Schwelle für das Gleichgewichtsorgan erfordert, wenn man vestibuläre Schäden ausschließen will, eine noch stärkere Herabsetzung des Streptomycinspiegels. Hierzu genügt Ozothin *allein offenbar* nicht.

Die Tatsache, dass Ozothin bei etwas stärker wirkenden Substanzen, wie z.B kanamycin, ebenfalls keinen Schutzeffekt mehr besitzt, könnte auf die gleiche Weise erklärt werden. Tyberghein kam nach eingehenden Untersuchungen zu der Feststellung, dass Ozothin nicht in der Lage ist, die Abnahme der Mikrophonpotentiale zu *verhindern. Er* glaubt sogar unter Ozothin eher stärkere Schädigungen gesehen zu haben

Zu dem gleichen Ergebnis gelangte kürzlich auch J P Brun, der bei quantitativen, histologischen Untersuchungen an *Cytocochleogrammen* unter Kanamycinsulfat, ohne und mit Ozothin, die gleichen Haarzellschädigungen sah.

Trotz diese negativen Beurteilungen des Ozothins kann man, im Hinblick auf die nachgewiesene konzentrati nsverminderung der toxischen Antibiotika sagen, Ozothin vermag zwar in geringem Umfang, ototoxische Schäden zu verhüten.

Es ist aber nicht in der Lage, Streptomycin zu entgiften. Eine Entgiftung

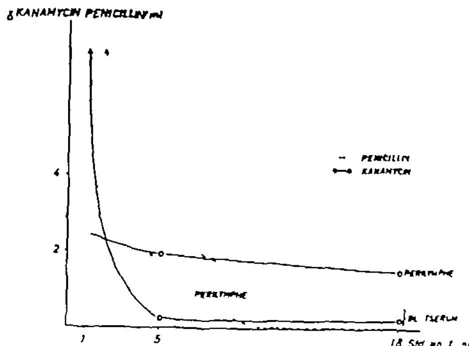


Abb. 18. Vergleich der Blut- und Perilymphkonzentrationen bei *niedriger Kanamycin-* (25 mg/kg) und 10fach höherer Penicillindosis (250 mg/kg)

im strengen Sinne liegt erst vor, wenn es gelingt, bei gleich hohem Antibiotikaspiegel, d. h. unter Erhaltung der vollen therapeutischen Wirkung, die toxische Eigenschaft dieser Substanzen zu vermindern. Diese Anforderung scheint auch Ozothin, soweit man dieses nach den Antibiotikakonzentrationen beurteilen kann, nicht zu erfüllen. Ein derartiger Effekt, wie wir *ihn bei Ozothin sehen, läßt sich wahrscheinlich ebenso durch eine entsprechend niedrigere Streptomycindosis erzielen.*

In diesem Zusammenhang muß hier festgestellt werden, daß Ozothin die antibiotische Aktivität der Streptomycesantibiotika auf Bakterienkulturen in vitro nicht beeinflußt. Es bedeutet aber nicht viel, wenn Mückter darauf verweist, daß eine Verminderung der therapeutischen bzw. antibiotischen Wirksamkeit *durch Ozothin experimentell an chronisch tuberkuloseinfi*zierten Tieren ebenfalls nicht beobachtet werden konnte. Man darf hierbei nicht übersehen, daß es sich in diesen tierexperimentellen Fällen um relativ grobe Untersuchungsmethoden mit großen Fehlerbreiten handelt. Die Auswirkung einer 20–25%igen Konzentrations- oder Dosisverminderung kann mit dieser Methode überhaupt nicht erfaßt werden. Daß eine Konzentrationsverminderung, wie sie nachweislich vorliegt, sei es auch nur um 20%, für die Therapie, wie Mückter meinte, belanglos sein soll, ist schwer einzusehen. Wenn dies der Fall wäre, müßte man zu Recht fragen, warum wird dann nicht einfach statt wie bisher üblich 1 g Streptomycin nur 0,8 verabreicht. *Da sich die therapeutische Dosierung,* wie wir sahen, bereits im Bereich der toxischen Schwelle bewegt, würde möglicherweise schon diese Reduzierung der Dosis ausreichen, um den kritischen toxischen Schwellenbereich zu vermeiden.

Wie soll man die Wirkungsweise des Ozothins erklären? Man neigt zu der Auffassung, dass ätherische Öle, wozu auch Ozothin zu rechnen ist, ähnlich wie andere Öle die Resorption des Antibiotikums an der Injektionsstelle verzögern, also eine Depotwirkung ausüben.

In diesem Fall müßte man aber einen anderen Verlauf des Blutspiegels erwarten, als ihn Abb. 17 zeigt. Die Blutkonzentrationskurve läge zwar niedriger würde dafür aber breiter d. h., zeitlich protrahierter verlaufen. Der Streptomycinspiegel des *Blutes unter Ozothin* überschneidet jedoch zu keinem Zeitpunkt die normale Streptomycinkonzentrationskurve, sondern bleibt stets unter dieser Das bedeutet, ein Teil des verabfolgten Streptomycins gelangt nicht in die Blutbahn. Über den Verbleib und das Schicksal des *restlichen Streptomycins* weiß man bis heute nichts.

Schwieriger ist die Deutung der unverhältnismäßig niedrigen Organkonzentration. Die Annahme liegt nahe, daß die membranabdichtende Wirkung der ätherischen Öle, die schon ohnehin erschwerte Aufnahme des Streptomycins in die Zellen der Organe verhindert. Ein Membraneffekt wäre ebenfalls zur Erklärung der behinderten Resorption am Injektionsort in Betracht zu ziehen. Auch im Innenohr könnte auf diese Weise ein Eindringen des Streptomycins von der Perilymphe in die Sinnesepithelien erschwert sein und dadurch u U sogar eine Schutzwirkung erklärt werden. Für diese mehr spekulativen Annahmen gibt es jedoch bis jetzt keine Beweise Erwiesen ist nur daß Ozothin den Antibiotikaspiegel herabsetzt und in geringem Umfang toxische Hörschäden durch Streptomyceesantibiotika zu verhindern vermag.

IX. Die Konzentrationen nicht ototoxischer Antibiotika, des Polymyxins Tetracyclins und Penicillins im Innenohr und anderen Organen

Auf Grund dieser Befunde sollte man nun erwarten, daß sich alle Stoffe mit ähnlichen Permeationseigenschaften wie die Aminoglykosidantibiotika im *Innenohr in gleicher Weise verhalten*. Demnach müßten sämtliche nicht resorbierbaren Substanzen in den Innenohrräumen eine relative Anreicherung erfahren. Bei Inulin fanden wir diese Analogie zwar bestätigt Mückter wies aber auf eine andere Antibiotikagruppe, die Polymyxine hin, die diese Anforderungen offensichtlich nicht *erfüllen. Obwohl die Polymyxine* wie das Colistin (Polymyxin E) sehr toxisch sind und außerdem die Eigenschaft besitzen, nicht resorbierbar zu sein, rufen sie bemerkenswerterweise keine ot toxischen Erscheinungen, sondern nur allgemeine neurotoxische Symptome hervor Das Verhalten des Colistins wurde von Mückter als Bewei dafür angeführt, daß unsere Auffassung nicht zutrifft und die schlechte Resorbierbarkeit offenbar für die Kumulation im Inneohr und für die totoxische Wirkung ohne Bedeutung ist. Diese Tatsache schien vielmehr die bis heute vorherrschende Hypothese von einer spezifischen

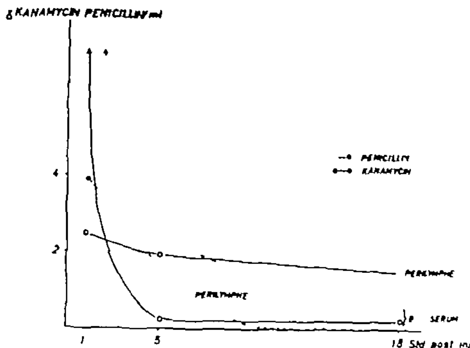


Abb 18 Vergleich der Blut und Perilymphkonzentrationen bei niedriger Kanamycin (25 mg kg) und 10fach höherer Penicillin dosis (250 mg/kg)

im strengen Sinne liegt erst vor wenn es gelingt bei gleich hohem Antibiotikaspiegel d h unter Erhaltung der vollen therapeutischen Wirkung, die toxische Eigenschaft dieser Substanzen zu vermindern Diese Anforderung scheint auch Ozothin soweit man dieses nach den Antibiotikakonzentrationen beurteilen kann, *nicht zu erfüllen Ein derartiger Effekt* wie wir ihn bei Ozothin sehen läßt *sich wahrscheinlich ebenso durch eine* entsprechend niedrigere Streptomycindosis erzielen

In diesem Zusammenhang muß hier festgestellt werden daß Ozothin die antibiotische *Aktivität* der Streptomycesantibiotika *auf Bakterienkulturen* in vitro nicht beeinflußt. *Es bedeutet aber nicht viel* wenn Mückter darauf verweist daß eine Verminderung der therapeutischen bzw antibiotischen Wirksamkeit durch Ozothin experimentell an chronisch tuberkuloseinfizierten Tieren ebenfalls nicht beobachtet werden konnte. Man darf hierbei nicht übersehen, daß es sich in diesen tierexperimentellen Fällen um relativ grobe Untersuchungsmethoden mit großen Fehlerbreiten handelt Die Auswirkung einer 20–25%igen Konzentrations oder Dosisverminderung kann mit dieser Methode überhaupt nicht erfaßt werden Daß eine Konzentrationsverminderung, wie sie nachweislich vorliegt sei es auch nur um 20% für die Therapie, wie Mückter meinte belanglos sein soll, ist schwer einzusehen *Wenn dies der Fall wäre müßte man zu Recht fragen* warum wird dann nicht einfach statt wie bisher üblich 1 g Streptomycin nur 0 8 verabreicht Da sich die therapeutische Dosierung, wie wir sahen, *bereits im Bereich der toxischen Schwelle bewegt würde möglicherweise* schon diese Reduzierung der Dosis ausreichen, um den kritischen toxischen Schwellenbereich zu vermeiden

1963 Fellers und Lindquist, 1964 Zimmermann und Werther 1964 Wegienka und Wellers, 1964 Sulkowski und Haserick, 1964 Mavromatis, 1965) auch zu Innenohrschädigungen führen würden, wenn sie in das Innenohr eindringen könnten. Für die Praxis bedeutet dieser Befund, daß Polymyxine und Tetracycline für eine *parenterale Behandlung* entzündlich bakterieller Innenohrerkrankungen wenig geeignet sind, dafür aber andererseits den großen Vorzug besitzen, keine ototoxische Nebenwirkung zu haben. Das schließt jedoch nicht aus, daß bei ihrer lokalen Anwendung vor allem bei einer offenen Paukenhöhle und großen Radikal oder Fensterungshöhlen, wo sie in unmittelbare Nähe des Innenohres gelangen, durch *Diffusion toxisch wirksame Antibiotikamengen* in das Innenohr gelangen und Schädigungen hervorrufen können. Für die Polymyxine und möglicherweise auch für die Tetracycline gilt grundsätzlich das gleiche wie für die toxischen Streptomycesantibiotika. Voraussetzung für ihre Ototoxizität ist, daß sie in einer toxisch wirksamen Konzentration den Schädigungsort erreichen So konnten Koide, Hata und Hando (1966) z. B tierexperimentell zeigen, daß sogar Chloramphenicol, wenn es in die Paukenhöhle unmittelbar vor das runde Fenster appliziert wird, ähnliche Innenohrschädigungen hervorruft wie Kanamycin oder Dihydrostreptomycin.

Die vorliegenden Befunde, das darf man zusammenfassend sagen, machen eine Korrektur der bisherigen Vorstellungen von der spezifischen Sensibilität des Innenohres gegenuber den Aminoglykosidantibiotika erforderlich. „Spezifisch kann wahrscheinlich nur der Kumulationsprozeß im Innenohr genannt werden. Wir kennen keine anderen Pharmaka, die in einer solch hohen Konzentration im Innenohr vorkommen wie die Antibiotika der Oligosaccharidgruppe. Selbst Penicillin, das für seine gute Liquorgängigkeit bekannt ist, fand sich in den Innenohrflüssigkeiten nur in vergleichsweise geringen Konzentrationen, die niemals den Blutspiegel übertrafen (Abb. 18) Charakteristisch für die Streptomycesantibiotika ist, daß sie selbst bei niedrigster nicht toxischer Dosierung, wie die Abb. 18 zeigt, im Innenohr einen höheren Spiegel aufweisen können als im Blut.

Die vorliegenden Befunde sollen zeigen, daß bei der Untersuchung der Otot xikosen genau wie bei jeder anderen Intoxikation die Frage nach der Konzentration der toxischen Substanzen am *Anfang aller* Überlegungen stehen sollt Sie alleine vermag schon vieles zu erklären, das gilt sowohl in therapeutischer Hinsicht als auch für die Giftwirkung und nicht zuletzt für die Bemühungen um eine Entgiftung. Das Wort Pharmakon hat in der griechischen Sprache einen doppelten Sinn. Es bedeutet Arznei und Gift. Paracelsus sagte der einzige Unterschied, ob ein Ding ein Gift sei oder nicht, liege in der Dosis. Diese alte Erkenntnis ist gerade im Hinblick uf die Streptomycesantibiotika von Bedeutung, weil hier die therapeutisch und toxisch Dosis dicht nebeneinander liegen und eine *Abgrenzung* zwischen Arznei und Gift besonders schwierig ist

TABELLE 4 *Colistinkonzentration nach einer einmaligen Injektion von 75 mg Colistin/kg*

Stunden post inj	Blutserum (γ/ml)	Herz (γ/g)	Leber (γ/g)	Gehirn (γ/g)	Perilymphe (γ/ml)
1	203,75 ± 106	2,1 ± 3,0	0,34 ± 0,23	0,03 ± 0,02	—
5	10,0 ± 7,4	0,2 ± 0,14	0,1 ± 0,069	—	—
18	0,18 ± 0,02	—	0,02	—	—
25	0,15 ± 0,06	—	0,07	—	—

Sensibilität des Innenohres gegenüber den Aminoglykosidantibiotika zu stützen.

Die Frage, warum Colistin nur neuro-, nicht aber ototoxisch ist, stellt, wie eine Untersuchung der Colistinspiegel ergab, ausschließlich ein Konzentrationsproblem dar (Tab. 4).

Es zeigte sich, daß die Polymyxine eine wesentliche Voraussetzung für eine Kumulation im Innenohr und für eine ototoxische Wirkung nicht erfüllen. Wie aus der Tabelle hervorgeht, kann Colistin offensichtlich nicht vom Blut in den Perilymphraum übertreten, ebensowenig wie es die Blut-Liquorschranke zu passieren vermag.

Eine ähnliche Erscheinung konnte bei den Tetracyclinen festgestellt werden (Tab. 5). Auch sie können bekanntlich die Blut-Liquorschranke nicht überschreiten. Genausowenig sind sie in der Lage, wie die Tabelle zeigt, die Blut-Lymphschranke zum Innenohr zu überwinden.

Dagegen kommen Tetracycline in allen anderen Organen sogar in relativ hohen Konzentrationen vor. Über die Blut-Liquor- bzw. Blut-Lymphschranke bestehen noch keine konkreteren Vorstellungen. Es wird auf Grund der unterschiedlichen Zusammensetzung des Liquors und der Innenohrlymphe angenommen, daß es sich um zwei verschiedene Schranken handelt. Sicher kann man aber sagen, daß die Molekülgröße alleine nicht zur Erklärung ausreicht, da wesentlich größere Moleküle wie Inulin und Albumin ohne Schwierigkeiten in das Innenohr gelangen.

Es wäre durchaus vorstellbar, daß die Tetracycline ähnlich wie sie in der Niere Zerstörungen der Tubuli hervorrufen (Cross, 1963, Frimpter

TABELLE 5 *Tetracyclinkonzentration nach einer einmaligen subkutanen Injektion von 100 mg Tetracyclin HCl/kg*

Stunden post inj	Blutserum (γ/ml)	Herz (γ/g)	Leber (γ/g)	Gehirn (γ/g)	Perilymphe (γ/ml)
1	11,0 ± 1,75	3 ± 0,2	3,7 ± 0,6	—	
5	[illegible]7 ± 1,65	[illegible],05 ± 0,37	1,0 ± 0,15	—	
18	1,33 + 0,06	0,8[illegible] ± 0,21	0,61 ± 0,8	—	
25	0,02 ± 0,7	0,38 ± 0,00	0,3 ± 0,01	—	

Konzentrationszeitverlauf, insbesondere auf den Innenohrspiegel der Aminoglykosidantibiotika haben. Aufgrund dieser Untersuchungen muß man annehmen, daß der Schutzeffekt des Oxothins wahrscheinlich auf der signifikanten Abnahme der Antibiotikakonzentration sowohl im Serum als auch im Innenohr und anderen Organen beruht. Die unterschiedliche Toxizität der einzelnen Pantothenat und Sulfatverbindungen der Oligomycesantibiotika läßt sich wahrscheinlich ebenfalls auf ihre verschieden hohen Konzentrationen in der Innenohrlymphe zurückführen. Demnach scheint es sich nicht um eine echte Entgiftung, sondern lediglich um eine Konzentrations- bzw Wirkungsminderung der toxischen Antibiotika zu handeln.

Diese Befunde machen eine Korrektur der bisherigen Vorstellungen über die spezifische Sensibilität des Innenohres erforderlich. „Spezifisch kann nur der charakteristische Kumulationsprozess der Aminoglykosidantibiotika im Innenohr genannt werden. An der Darmmucosa der Ratte läßt sich demonstrieren, daß auch hier wenn die toxischen Substanzen nur in einer entsprechend hohen Konzentration einwirken, ein histologisch sehr ähnliches Schädigungsbild der oberflächlichen Epithelschicht hervorgerufen wird, wie es von der Niere und dem Innenohr her bekannt ist. Sowohl die spezifisch-ototoxische Wirkung als auch die „Entgiftungs-Versuche der Aminoglykosidantibiotika können im wesentlichen als Konzentrationseffekte erklärt werden.

D ZUSAMMENFASSUNG

Keine der zahlreichen Theorien über die toxische Wirkungsweise der Aminoglykosidantibiotika vermag zu erklären, warum ausschließlich das Innenohr und die Niere geschädigt werden, während alle anderen Organe verschont bleiben. Man begnügte sich mit der Annahme, daß die Zellen des Innenohres eine spezifische Sensibilität gegenüber diesen Substanzen besitzen. Diese wenig befriedigende Hypothese war Anlaß, nach weiteren Ursachen zu forschen.

Eine Untersuchung der Verteilung und des Konzentrations-Zeit-Verlaufs der *toxischen Streptomycesantibiotika beim Meerschweinchen* brachte folgende Ergebnisse:

Alle Antibiotika der Aminoglykosidgruppe, sowohl Streptomycin und Dihydrostreptomycin als auch *Kanamycin und Neomycin werden in der* Peri- und Endolymphe des Innenohres angereichert und retiniert. Ihre Konzentration im Innenohr und in der Niere übertrifft alle anderen Organe und sogar den Blutspiegel um ein Vielfaches. Je toxischer die Substanzen sind, umso ausgeprägter ist auch ihre Kumulation in der Innenohrlymphe. Offensichtlich besteht eine Relation zwischen der Konzentration und der Ototoxizität der verschiedenen Aminoglykosidantibiotika.

Schon in niedriger, nicht toxischer Dosierung erreichen die Antibiotika der Aminoglykosidgruppe einen relativ hohen Innenohrspiegel. Die Ursache hierfür ist wahrscheinlich in einer erschwerten Elimination und Retention der praktisch nicht resorbierbaren Substanzen dieser Antibiotikagruppe in den Innenohrräumen zu sehen. Eine vergleichbare Kumulation fand sich auch bei Inulin, das hinsichtlich seiner Verteilung im Organismus ähnliche pharmakologische Eigenschaften aufweist wie die toxischen Streptomycesantibiotika. Darüber hinaus kommt es mit Überschreiten der toxischen Schwelle noch zu einer weiteren unverhältnismässig starken Zunahme der *Innenohrkonzentration der Aminoglykosidantibiotika.* Dieser letzte Vorgang, den man im Gegensatz zur normalen Kumulation als toxisch bedingten Kumulationsprozess bezeichnen kann, ist wahrscheinlich auf eine Störung der Membranpermeabilität zurückzuführen.

Andere Antibiotika, wie Penicillin, erreichen vergleichsweise nur einen minimalen Innenohrspiegel, während *Tetracyclin und Erythromycin* B (Gelbstin®) überhaupt nicht in das Innenohr einzudringen vermögen und darum auch nicht ototoxisch wirken können.

In diesem Zusammenhang wurde weiterhin die Frage zu klären versucht, ob Substanzen wie Pantothensäure oder Oxythin, die angeblich die Toxizität der Streptomycesantibiotika herabsetzen sollen, einen Einfluß auf den

Konzentrationszeitverlauf insbesondere auf den Innenohrspiegel der Aminoglykosidantibiotika haben. Aufgrund dieser Untersuchungen muß man annehmen, daß der Schutzeffekt des Ozothins wahrscheinlich auf der signifikanten Abnahme der Antibiotikakonzentration sowohl im Serum als auch im Innenohr und anderen Organen beruht. Die unterschiedliche Toxizität der einzelnen Pantothenat und Sulfatverbindungen der Oligomycesantibiotika läßt sich wahrscheinlich ebenfalls auf ihre verschieden hohen Konzentrationen in der Innenohrlymphe zurückführen. Demnach scheint es sich nicht um eine echte Entgiftung, sondern lediglich um eine Konzentrations- bzw. Wirkungsminderung der toxischen Antibiotika zu handeln.

Diese Befunde machen eine Korrektur der bisherigen Vorstellungen über die spezifische Sensibilität des Innenohres erforderlich. „Spezifisch" kann nur der charakteristische Kumulationsprozess der Aminoglykosidantibiotika im Innenohr genannt werden. An der Darmmucosa der Ratte läßt sich demonstrieren, daß auch hier wenn die toxischen Substanzen nur in einer entsprechend hohen Konzentration einwirken, ein histologisch sehr ähnliches Schädigungsbild der oberflächlichen Epithelschicht hervorgerufen wird, wie es von der Niere und dem Innenohr her bekannt ist. Sowohl die spezifisch-ototoxisch Wirkung als auch die „Entgiftungs-Versuche" der Aminoglykosidantibiotika können im wesentlichen als Konzentrationseffekte erklärt werden.

6 *01043 Stupp

E SUMMARY

None of the many theories on the toxic mode of action of the amino-glycoside antibiotics can account for the injuries done solely to both the inner ear and the kidney while all other organs remain unaffected. The mere assumption, that the cells of the inner ear show a specific sensitivity towards these substances, seemed to be a sufficient answer. However this rather unsatisfactory hypothesis gave rise to search for additional causes.

Following are the results obtained from a study on the distribution and the time of concentration of the toxic streptomyces antibiotics in the guinea pig.

All antibiotics belonging to the group of amino-glycosides, including streptomycin and dihydrostreptomycin as well as kanamycin and neomycin, are concentrated and retained in the inner ear fluids. Their concentration both in the inner ear and the kidney exceeds that of all other organs, even of the blood level, many times over. The higher the toxicity of the substances, the more intense is their accumulation in the inner ear fluid.

Evidently there exists a relation between the concentration and the ototoxicity of the different amino-glycoside antibiotics.

Even a small and non toxic dose of the antibiotics of the amino-glycoside group will suffice to reach a relatively high level in the inner ear. The reason for this may be looked for in a complicated elimination and retention of the practically non absorbable substances of this particular group of antibiotics in the inner ear spaces. Also a comparable accumulation could be observed when administering inulin which with respect to its distribution in the quinea pig showed similar pharmacological properties like the toxic streptomyces antibiotics. In addition, on over-stepping the threshold to toxicity another excessive increase of the amino-glycoside antibiotics of the inner ear concentration could be noticed. The last procedure which in contrast to the normal accumulation may be designated as a toxic conditioned accumulation process, is likely to result from a disturbance of the membrane permeability.

In comparison other antibiotics like penicillin attain only the lowest level of the inner ear while tetracycline and polymyxin F (Colistin®) will not penetrate into the inner ear at all, thus lacking the ototoxic effect.

In this connection an attempt has been made to settle the point of question whether substances like pantothenic acid or ozothin which are supposed to diminish the toxicity of the streptomyces antibiotics, take an influence on the concentration, particularly on the inner ear level of the amino-glycoside antibiotics. On the basis of these examinations, one is

inclined to believe that the protective action of oxothin has probably been created by the significant decrease in the antibiotic concentration both in the serum, the inner ear and other organs. The varying toxicity of the individual pantothenic and sulfate combinations of the oligomyces antibiotics may also be explained by their differing concentrations in the inner ear fluid. Hence, it seems not to be a question of an authentic detoxication, but merely a matter of a decrease in concentration, respectively of a reduced effect of the toxic antibiotics.

These findings make a correction of the previous concepts about the specific sensitivity of the inner ear indispensable. The designation Specific" can only be given to the characteristic process of accumulation of the amino-glycoside antibiotics in the inner ear The results obtained from a study of the intestinal mucosa of rats showed that here also, when the toxic substances administered in a correspondingly high concentration take effect, a similar picture of the injuries done to the superficial epithelial layer is created, as is known to exist in the kidney and the inner ear Both the specific-ototoxic effect, as well as the detoxication tests of the amino-glycoside antibiotics, may essentially be defined as concentration effects.

F RÉSUMÉ

Des nombreuses théories sur le mode d'action toxique des antibiotiques du genre aminoglucoside, aucune ne peut expliquer pourquoi exclusivement l'oreille interne et le rein sont atteints, alors que tous les autres organes ne le sont pas. On se contentait d'accepter que les cellules de l'oreille interne possèdent envers ces substances une sensibilité spécifique. Cette hypothèse peu satisfaisante fut la raison de rechercher d'autres causes de cette activité spécifique.

Une recherche de la répartition et de l'écoulement en fonction du facteur concentration-temps des antibiotiques streptomyciniques toxiques dans le cobaye donna les résultats suivants,

Tous les antibiotiques du groupe des aminoglucosides, aussi bien la streptomycine et la dihydrostreptomycine que la kanamycine et la néomycine s'accumulent dans les liquides de l'oreille interne et y sont rétentionnés. Leur concentration dans l'oreille interne et dans les reins surpasse de plusieurs fois celle dans tous les autres organes et même celle dans le sang.

Plus ces substances sont toxiques, plus leur accumulation dans les liquides de l'oreille interne est élevée. Il y a apparemment une relation entre la concentration et l'ototoxicité des divers antibiotiques du genre aminoglucosides.

Les antibiotiques du groupe des aminoglucosides atteignent déjà à faibles doses atoxiques un niveau relativement élevé dans l'oreille interne. La cause en est vraisemblablement une élemination plus difficile et une rétention des substances pratiquement irrésorbables dans les espaces de l'oreille interne de ce groupe d'antibiotiques. Une accumulation comparable fut trouvée avec l'inuline, qui présente au point de vue de sa répartition dans l'organisme des propriétés pharmacologiques semblables à celles des antibiotiques streptomyciniques. En plus, avec le dépassement du seuil de toxicité survient encore une augmentation disproportionée de la concentration des antibiotiques du genre aminoglucoside dans l'oreille interne. Ce dernier phénomène que l'on peut à l'encontre d'une accumulation normale, décrire comme étant un processus de cumulation dû à la toxicité est probablement à attribuer à une dérangement de la perméabilité des membranes.

D'autres antibiotiques, comme la pénicilline n'atteignent en comparaison qu'un niveau minimal dans l'oreille interne alors que la tétracycline et la polymyxine F (colistine*) ne sont absolument pas capables de pénétrer dans l'oreille interne et ne peuvent par conséquent non plus avoir d'activité ototoxique.

Dans ce contexte on chercha alors à résoudre la question de savoir si des substances comme l acide pantothénique ou l'ozothine, qui prétendûment doivent diminuer la toxicité des antibiotiques streptomyciniques, ont une influence sur l écoulement en fonction du facteur concentration-temps des antibiotiques du genre aminoglucoside et particulièrement sur le niveau qu'ils atteignent dans l oreille interne. D après ces recherches, on doit admettre que l'effet de protection de l ozothine est vraisemblablement basé sur la diminution significative de la concentration d antibiotique aussi bien dans le sérum que dans l'oreille interne et d autres organes. On peut *probablement* aussi attribuer la toxicité différente de chaque composé pantothénique et sulfurique des antibiotiques oligomycétiques à leur concentration différemment élevée dans les liquides labyrinthiques.

D'après cela, il ne s agirait pas d une véritable désintoxication, mais purement et simplement d une diminution de la concentration, respectivement de l'activité, des antibiotiques ototoxiques.

Ces résultats rendent nécessaire une correction des anciennes notions sur la sensibilité spécifique de l oreille interne. On ne peut nommer spécifique que le processus caractéristique d accumulation des antibiotiques du genre aminoglucoside dans l'oreille interne. On peut démontrer au niveau de la muqueuse intestinale du rat, que là aussi, lorsque les substances toxiques agissent dans une concentration relativement élevée, elles provoquent une forme de lésion de la couche épithéliale superficielle, histologiquement très analogue à celle que l'one connait au niveau du rein et de l'oreille interne. L activité spécifiquement ototoxique, aussi bien que les recherches de désintoxication des antibiotiques du genre aminoglucoside, peuvent être expliqués comme étant essentiellement des effets de concentration.

F RÉSUMÉ

Des nombreuses théories sur le mode d'action toxique des antibiotiques du genre aminoglucoside, aucune ne peut expliquer pourquoi exclusivement l'oreille interne et le rein sont atteints, alors que tous les autres organes ne le sont pas. *On se contentait d'accepter que les cellules de l'oreille interne possèdent envers ces substances une sensibilité spécifique.* Cette hypothèse peu satisfaisante fut la raison de rechercher d'autres causes de cette activité spécifique.

Une recherche de la répartition et de l'écoulement en fonction du facteur concentration-temps des antibiotiques streptomyciniques toxiques dans le cobey donna les résultats suivants.

Tous les antibiotiques du groupe des aminoglucosides, aussi bien la streptomycine et la dihydrostreptomycine que la kanamycine et la néomycine s'accumulent dans les liquides de l'oreille interne et y sont rétentionnés. Leur concentration dans l'oreille interne et dans les reins surpasse de plusieurs fois celle dans tous les autres organes et même celle dans le sang.

Plus ces substances sont toxiques, plus leur accumulation dans les liquides de l'oreille interne est élevée. Il y a apparemment une relation entre la concentration et l'ototoxicité des divers antibiotiques du genre aminoglucosides.

Les antibiotiques du groupe des aminoglucosides atteignent *déjà à faibles* doses atoxiques un niveau relativement élevé dans l'oreille interne. La cause en est vraisemblablement une élémination plus difficile et une rétention des substances pratiquement irrésorbables dans les espaces de *l'oreille interne de ce groupe d'antibiotiques. Une accumulation comparable* fut trouvée avec l'inuline, qui présente au point de vue de sa répartition dans l'organisme des propriétés pharmacologiques semblables à celles des antibiotiques streptomyciniques. En plus, avec le dépassement du seuil de toxicité survient encore une augmentation disproportionée de la concentration des antibiotiques du genre aminoglucoside *dans l'oreille interne*. Ce dernier phénomène, que l'on peut à l'encontre d'une accumulation normale, décrire comme étant un processus de cumulation dû à la toxicité est probablement à attribuer à une dérangement de la perméabilité des membranes.

D'autres antibiotiques, comme la pénicilline, n'atteignent en comparaison qu'un niveau minimal dans l'oreille interne alors que la tétracycline et la polymyxine E (*colistine®*) ne sont absolument pas capables de pénétrer dans l'oreille interne et ne peuvent par conséquent non plus avoir d'activité ototoxique.

Dans ce contexte on chercha alors à *résoudre la question de savoir si* des substances comme l acide pantothénique ou l oxothine, qui prétendûment doivent diminuer la toxicité des antibiotiques streptomyciniques, ont une influence sur l'écoulement en fonction du facteur concentration-temps des antibiotiques du genre aminoglucoside et particulièrement sur le niveau qu'ils atteignent dans l'oreille interne. D'après ces recherches, on doit admettre que l'effet de protection de l'oxothine est vraisemblablement basé sur la diminution significative de la concentration d antibiotique aussi bien dans le sérum que dans l'oreille interne et d'autres organes. On peut *probablement* aussi attribuer la *toxicité* différente de chaque composé pantothénique et sulfurique des antibiotiques oligomycétiques à leur con centration différemment élevée dans les liquides labyrinthiques.

D après cela, il ne s agirait pas d'une véritable désintoxication, mais purement et simplement d une diminution de la concentration, respectivement de l activité, des antibiotiques ototoxiques.

Ces résultats rendent nécessaire une correction des anciennes notions sur la sensibilité spécifique de l oreille interne. On ne peut nommer spécifique que le processus caractéristique d'accumulation des antibiotiques du genre aminoglucoside dans l'oreille interne. On peut démontrer au niveau de la muqueuse intestinale du rat, que là aussi, lorsque les substances toxiques agissent dans une concentration relativement élevée, elles provoquent une forme de lésion de la couche épithéliale superficielle, histologiquement très analogue à celle que l'one connaît au niveau du rein et de l'oreille interne. L activité *spécifiquement ototoxique*, *aussi bien* que les recherches de désintoxication des antibiotiques du genre aminoglu coside, peuvent être expliqués comme étant essentiellement des effets de concentration.

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SUPPLEMENTUM 61

THE LARYNX,
ORGAN OF VOICE

BY

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Translated from the Latin
with preface and anatomical notes
by
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UPPSALA 1969

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CONTENTS

TRANSLATORS' PREFACE

De vocis auditusque organi historia anatomica by Juli s Casseriu (1561–1616) wa published by Victorius Baldinus in Ferrara i 1601 The f ll consists f two treatises, the first dealing with the lary x and the second with the ea The section on the lary consist of 191 pages with 22 plates. Copper plates were used d were probabl drawn and etched by the Swiss painter Joseph Murer or Maurer

Th tran lators of this work employed microfilm facsimile obtained from the Armed Forces Medical Library (Acc. No. 10506) Since there ppears to be no English translation of Casseriu book, an initial literal translatio wa m de by I H Hamark. Then, M. Hast read the literal translation editing the same for an scientific l ccuracies, particula ly of an anatomical n ture. Finally the tw translators combined their respective t lents t obtain a more finished tra s-lation of thi "Renai sance medical w k. Where required, th modern termin l-ogy for a structure l given, employing the nomenclature adopted by the I.A.N.C. a d presented in their 1960 publication of the *Nomina Anatomica.*

Th treatise on the laryn l composed of the author" expected serenissimo to his patron, epigrams, pref e bibliography and index, followed by the body of three books. Casseriu not only deals with structure and f ction f the laryn of huma and domestic animals, but he also devotes a large portion of hi work to describi g theories of th voice For Casserius, the larynx *is* the rg n of voice d thi i it "purpose i the bod Because of strong interest one of u (M H st) h f the natomy of the muscles nd nerves of the larynx, we ha e con-fined our translation, for the present, t the first eight hapters of Book I.

Lik hi contemporaries and teachers, Casserius w greatly influenced by Galen. Which ideas or observation are origi al to Casserius or must be attributed t Galen i debat ble Certai ly Casserius discussion of th n echanism of the recurrent nerves is Galeni (*De Usu Partium*) But the detailed description Cas-seriu gi es f the lary geal muscles has n equal i th contemporary an tomy of hi day If he stood upon the shoulders of great men t see further as we all d s, d did not a knowledge their support, we should chastise him, but he i rarely guilty of thi fault. It is true that hi work does suffer from the inherited scholasti i m of the Middle Ages William H rvey's famous publication was twenty-seven years in the future d scientifi thi ki g was still teleological. But Casseri s, n lik man future students f anatomy could pproa h his work w thout th preconcei ed notions we all obtain from studyi g the standard t xt book of atomy (with their beautiful illustrations) guiding our knife on its proper course H learnt hi discipline by that i valuable but laborious method f maki g di sections by himself *Therefore if the* reader does not lways find Casseri description of the course of muscle s he would expect or was taught, let him return t the di secti g room with n unprejudiced mi d and without notes or t tbooks.

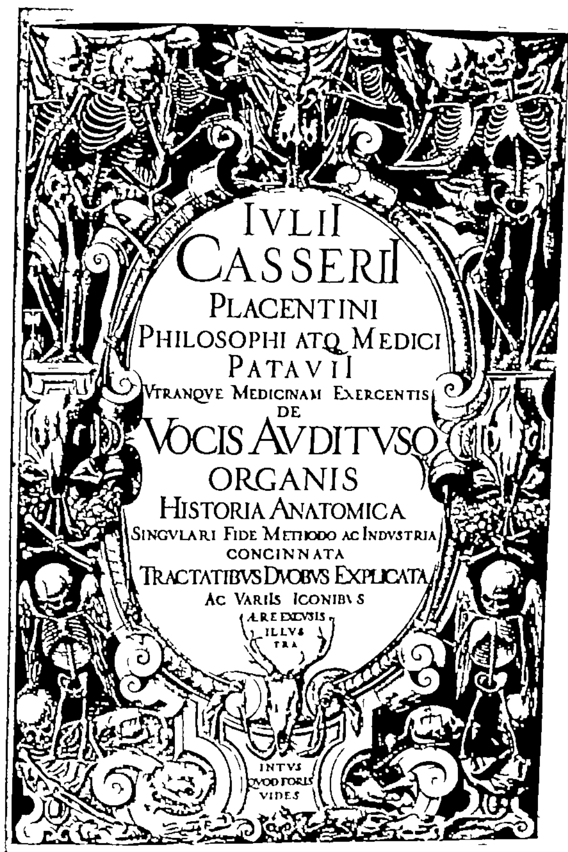
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De voci auditusque organi historia anatomica by Julius Casserius (1561–1616) was published by Victorius Baldinus in Ferrara in 1601. The folio consists of two treatises, the first dealing with the larynx and the second with the ear. The section on the larynx consists of 191 pages with 22 plates. Copper plates were used and were probably drawn and etched by the Swiss painter Joseph Murer or Maurer.

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The treatise on the larynx is composed of the author's expected sereal simo to his patron, epigrams, preface, bibliography and index, followed by the body of three books. Casserius not only deals with structure and function of the larynx of human and domestic animals, but he also devotes a large portion of his work to describing theories of the voice. For Casserius, the larynx *is* the organ of voice, and this is its purpose in the body. Because of a strong interest in one of us (M. H. H.) has in the anatomy of the muscles and nerves of the larynx, we have confined our translation, for the present, to the first eight chapters of Book I.

Like his contemporaries and teachers, Casserius was greatly influenced by Galen. Which ideas or observations are original to Casserius or must be attributed to Galen is debatable. Certainly Casserius' discussion of the "mechanism" of the recurrent nerves is Galen's (*De Usu Partium*). But the detailed description Casserius gives of the laryngeal muscles has no equal in the contemporary anatomy of his day. If he stood upon the shoulders of great men to see further as we all do, and did not acknowledge their support, we should chastise *him*, but he is rarely guilty of this fault. It is true that his work does suffer from the inherited scholasticism of the Middle Ages. William Harvey's famous publication was twenty-seven years in the future and scientific thinking was still teleological. But Casserius, unlike many future student of anatomy could approach his work without the preconceived notions we all obtain from studying the standard text books of anatomy (with their beautiful illustrations) guiding our knife on its proper course. He learnt his discipline by that invaluable but laborious method of making a dissection by himself. Therefore if the reader does not always find Casserius' description of the course of a muscle as he would expect or was taught, let him return to the dissecting room with an unprejudiced mind and without notes or textbooks.



F csimil of th Titl P g

AN ANATOMICAL HISTORY ON THE ORGANS OF VOICE AND HEARING

Harmoniously Arranged, With Outstanding and Faithful Precision and Care Discussed in Two Treatises Illustrated by Various Copper Printed Diagrams

by

JULIUS CASSERIUS OF PIACENZA
Philosopher and Physician at Padua
Practitioner of Theoretical and Applied Medicine

DE NERVIS RECURRENTIBUS
Caput VIII



ABSOLVTA itaque Musculorum Laryngis historia, ordo exigit ut Nervorum per quos movendi facultas musculis communicatur delineationem noster excipiat sermo; in eisque depingendis naturae ingentem solertiam summi Opificis industriam, nec non artificium, penè inessabile, lineis exprimam sui exilentissimus. Qui tam admirando modo à benignissimo omnium parente, Deo, & Natura, constructi sunt ut impudentissimos iudices nonnullos, qui secundariam illam rerum omnium matrem imperitia arguere, & novercam appellare, non erubuerunt, (cuius tamen, non dicam opere sed ne verbis quidem, providentiam, ac sagacitatem assequi, stupidissimo potuerunt ingenio) non possim non summopere admirari. Horum itaque Nervorum is est progressus ut alij transversim; alij obliquè; alij supernè exorti deorsum; alij infernè scaturientes sursum; alij sinistrorsum, dextrorsum alij repant & musculos ingrediantur. Tam vario incedunt ductu propter musculorum quos subeunt positionem. Nervi enim, non cuiuis musculi parti, possunt inseri; sed vel capiti tantum vel medio, (ventrem vulgo vocant) infra medium, ut fini, seu tendini; nihilominus implantari queunt; tunc quippe musculorum principium contractis fibris suis conditiones subiret. Omnes enim musculi versus suum principium (modo nervorum propagines suscipiant) perpetuò contrahuntur. Cum itaque alterutra tantum nervus in musculos contingat insertio; necessarium fuit ut tam variè procederent. Musculorum quidem alios, transversim positionem obtinere, obliquam magis nonnullos, reliquos verò recta, prout infernè sursum vel supernè deorsum spectant edocet Anatome. Porrò duo, supernè deorsum sese in duos Laryngis musculos duabus apophysibus insinuant. Earum productionum altera ad clatiorem Scutiformis cartilaginis partem tendens ipsi inseritur; altera ad obliquos musculos, & eos qui ad os pectorale exporrecti sunt commigrat. Ut duo hi musculi supernè descendunt; ita etiam duo nervi eorum gratia formati sunt qui ad positionem eorum progrediuntur. Musculi infernè sursum spectantes ut oppositi sunt prioribus, ita etiam opus fuit ab infernis partibus, ad superiores, nervos deriuare. Verum cum nervi omnes vel à Cerebro vel à Collo, seu Spinali medulla, emergant; non abs re erit tum ab vero principio Nervi per Laryngem dispersi originem trahant tum quomodò musculis implantentur, perquirere. Non à Collo seu à Spinali Cervicis medulla produci oportuit eò quod obliqui essent futuri. Et licet hoc non obstaret attamen aequum esset naturam non ab ignobiliori Nervorum principio, sed à digniori Laryngis, vocis organo principalissimo, Nervos impertiri: Quare à Cerebro. Caeterum Nervi à Cerebro prodeuntes, ex duobus à se invicem distantibus, ac distinctis fontibus scaturiunt; e porè à sexta vel septimae coniugationis Nervi. Ab his quidem nullo pacto diminare poterant, cum tantum obliqui inutiles omnino futuri essent: Ab illis itaque videlicet, sextae coniugationis Nervis qui per collum secundum utramque Tracheae partem rectà deorsum excurrentes paululum ab exortu suo progressi illicò in multas spargantur propagines; quarum nonnullae ad Thoracem ad Cor ad Pulmonem, Stomachum, nonnullae verò longius procedentes, ad Ventrem, Hepar Lienem & omnes ferè partes in Abdomine contentas serpunt. Verumenimverò,

I quia

The Three Books of the First Treatise on the Anatomical History of the Larynx, the Organ of Voice, by Julius Casserius of Piacenza, Philosopher, Physician and Anatomist

BOOK ONE ON THE STRUCTURE OF THE LARYNX, THE ORGAN OF VOICE

CHAPTER I

The Excellences of the Voice and its Worthiness methodology for treatment of topics

Because I have reviewed the usefulness of the subject which I am going to discu and have weighed it merits with careful deliberation, now as I set ut t con ider with utmost precision the instruments of voice and hearing (the larynx and the ear respectively) I sense a certain prompting to investigate a more important subject matter Fo it *seemed* a worth-while thing to make some prefatory remarks and bring into focus the *magnifi cence* as well as the purpose of each organ. The excellence of these *organs* merits much praise and honor since without them we could have neither voice nor hearing No flippancy then, is to be attributed to my intention to begin with that exqui ite h ndiwork of nature the organ of voice which Galen calls the larynx I shall attempt t outline to some degree of complete ness the xcellence utility and necessity of oice Thus each individual will h v thorough appreciation of the importance of a studied and accurate treatise on the larynx, of the value to be placed on such a work, and the need for it. For when the larynx is formed as nature intended, voice too is produced in a natural way but if the larynx is not shaped naturally voice is uttered in corrupted fashion and if the larynx is totally lacking, so is voice I hall speak not in a full oratorical style (for in proportion to the un peakabl richness of the material that appears in the celebration of voice it majestic dignity will shine forth, even like *the sun*, without the harmonio ly modulated sound of the word)—I shall speak, then, in a philosophi cal manner with bar and simple words. And such, as Euripides says, are the word proper of the truth. I shall, furthermore treat all the virtually countle topics which appear on this rich field of discourse For if I decided t peak in proportion to the abundance and fullness of the mate-

rial I would run out of paper and ink, by the gods, sooner than I would run out of something to say Suppose you were to review what the above mentioned individuals have, with the greatest wisdom handed down from ancient times about voice suppose you were to consider everything which we daily experience during our mortal lives suppose, finally you were to examine what has been sanctified on voice in our monuments of sacred literature—do this, and immediately the subject matter like an overflowing river will rush down on you resulting in the need for you to admit that you would be overwhelmed much more by the abundance of things to discuss than by the lack thereof Onward, then to trace our beginning from the writings left by the ancient philosophers! Is it not the case that Aristotle who is easily the foremost of all philosophers, seems to place before our eyes in a marvelous fashion the excellence, utility and necessity of voice? that along with Galen the keenest of investigators into nature s secrets, he announced that speech is the interpreter of our reasoning and intellect, the unfolder of all our conceptual throughts and, in like manner the active component of our soul? For our verbal expressions are the indices to the passions of our inner being (Periher first said that) It was perhaps with this understanding that Speusippus, a very important writer claimed in *Platonius definitionibus* that speech is an oral product in accord with our reasoning, and therefore it is judged to be no mean index to our emotions. On this account the Physiologists have agreed on the following equivalences if his voice is without force, it shows that the man is weak and timid if it is coarse, that he is deceitful and haughty if it is clear that he is clever and talented if it is heavy that he is brave and persevering if it is tremulous, that he is envious and lazy if it is deep that he is rash and harmful if it is rough harsh and changing, that he is a vain and flippant man who loves luxury and if it is gentle, that he is calm and withdrawn And so in the divine words of Plato just as the birds are distinguished by their song and jars by their sound so the talents and natural bents of men are recognized as distinct by their discourse Thus, when with many pleas, a certain man prevailed on Socrates to give a judgement about the character of a slave who had been brought before him, he said to him Speak, and I shall know you! By this comment he clearly indicated that a youth of distinguished prospects is most easily known from the way he talks It was indeed a comment worthy of so great a philosopher So Diogenes used to say that he always wondered why we rested content with a look only when buying a man but would buy a jar or some piece of handiwork only after touching it or listening to its sound Plutarch recounts an episode not dissimilar from this one in his Symposiacis, concerning the preeminent Simonides while the guests, eating and drinking were enjoying themselves at the table with jokes, witticisms and pleasantries, he would observe some individual who was lost in silent thought and saying nothing, and then assert that if this individual really was a wise man his silence was foolish, but that if he was a foolish man then it was wise Since, therefore our voices are indices of our inner

leanings, there is the greatest necessity to compare our thoughts about those matters and our knowledge For on the one hand our intellect endowed with such nobleness that it is not associated with any organs, is by its nature single immaterial and immortal and does not at all stand in need of the aid and help of the senses in order to exercise its function of understanding on the other hand, however it is closely connected to our mortal, solid and earthly body and, as the poet sings, earthly actions I lunt it—it is in fact so blunted by our moribund flesh that without the aid of the senses it could not attain to thought or knowledge. Consequently Plato was right in naming the senses the intermediaries and, as it were the servants of the mind, and saying that they were the guides that lead to the truth Please remember too, the claim of his student Aristotle nothing is understood except what has first been perceived by the senses, since they pave the way so to speak, f r understanding the matter in question." Therefore he established, in another work, that if any man should by nature be denied one of the senses from birth, he would necessarily lack some knowledge

Among all the senses two are especially suited f r gaining knowledge the eyes and the ears—the eyes have been established by nature herself t in estigate objects close at hand the ears, to hear of these objects when they are reported by somebody else But nature again, willed speech to be the instrument responsible for sharing and communicating the ideas of the mind. If someon therefore sh uld suddenly do away with speech, he, it seems, will have rem ved the instrument necessary for garnering knowledge, indeed, will h ve taken from the universe its sun, the very chief and guide of the tars. And not only innate and scientific skills need the aid of speech, *but the* arts of free man nd sla e cannot be taught, in fact, cannot even exi t or be practiced without speech. Should you set wood before the car penter and iron before the smith without telling them that they must fashion a bench or a key respectively from their materials, *all their labor* will have been undertaken in vain, for they will make no object from their materials. N r hould *one* jud*ge that it* would be any different in the case of government and magi tracies. For what is it that promulgates the laws necessary for th preservation of peace am ng men Speech What declares statutes Speech. What defends th innocent man *in the law-court*, acquits him of his accusation f wrong What charges the guilty *man*, proves the accusati n lodged against him condemn him, punishes him? Speech Speech, I say the preserver f peace and justice Speech is so loyal a companion and helpmeet of ju tice that it does not adjudge *defendents* without an open hearing of their case It raises up the oppressed and *lifts* high those who lie low It mean destruction for the wicked, protection for the innocent, terror for the base and delight for the upright. On this account the books claim, Ale ander the Great wa praised, since he refused to let that most abom inal le of men, I hilotas, be dragged *off* to his punishment before his defense had mad its plea—and that though *Philotas*, along with his father I rmenio and some other men, was forming a conspiracy to murder *Alex*

2 [illegible]

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To this day from the time of the Apostles and their successors, speech ha made the shining light of the Christian religion *flash forth*—not only in ur own lands, but in the rem test region of this great w rld the brilliance f th Faith has increased, th darknes of wrongs has been routed, the di grace f the cros has been done away with, the sacred and holy E angel of Christ ha been preached, heresies ha e been destroved and heretics compl tely laid low By means of peech the thanks due to God are rendered t Him and sacred prayers are offered up in our action we ask for he enly help nd in our difficulties we implore consolation and alleviation fr m God. By peech will thi universe one day be destroyed when the heav n di int grate in heat when the son of God appears in the clouds, the

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ander! On the supreme excellence of speech its marvelous usefulness! Speech renders service to writers of music comedy and tragedy as well as to orators. By its aid is commerce carried on it enters into contracts and breaks them *and it strengthens both those free of debt and those* whose fortunes have been shattered Speech calls men away from the way of the beasts and from their enormous savagery towards gentleness and an upright relationship in their dealings If men ever swerve from the straight path of life, speech leads them back onto the road of safety Speech points out men s spiritual *suffering and confusion but it also sets them in motion and allays* them Speech builds states, comforts the wretched causes marriages to come about carries on the business affairs of men and is judged to appoint an eternal peace among them We do not recognize, however speech as useful *and necessary only* in peace but also in war Speech proclaims the state of war to the enemy instructs us *to fight to the finish when engagements* have started, gives courage to the terrified and puts hostile squadrons to flight Oh Speech you gather soldiers together call back those who flee ease the burden of the overwhelmed stir your men to battle and strike panic terror in the hearts of the enemy And in this way alone it was the custom not only among the barbarians but also among the Romans to utter a shout before the attack and during the actual fighting to terrify the enemy and encouarge one s own side—and this is vouched for in the historical writings of Livy Tacitus and Caesar Therefore when Paulus Aemilius was teaching young men to fight intrepidly he used to say that the enemy were frightened and put to flight more by words and speech than by the sword and the hand Indeed Livy the distinguished historian wrote that the successful or un successful outcome of war was indicated on the evidence of speech shout ing, he says, was *the first index as to how the situation was likely to even* tuate—be it somewhat excited quite frequently answered by the enemy *different from that of the Romans, unequal lazy or repeated often* Finally nature, the parent of all things, recognized that so great was the usefulness of speech that she endowed living creatures with it or at least a sound very *similar to it* Thus they *could guard against harm* seek their living pursue pleasure and avoid difficulties men especially could be moved and stirred by sweet wheedling speech to propagate the species. How aptly and ad mirably does that plaintive voice of the owl unfold its inner feelings, pas sions and loves, and point up its anger The same is the case for the mourn ful sound of the kite the groaning plaints of the turtle-dove the repeated sound of the cuckoo the sweet chattering of the nightingale and the chirping of sparrows To such an extent do they seem in uttering their sounds, now to lament now to rejoice and, *again now to be looking for one thing* now to be asking for something else Nigthingales, moreover leave us no room for doubt on this matter about whom th poets tell here and there that they keep weeping for wrong suffered long ago—Martial in particular so relates. Philomela the nightingale beweeps her impious crime

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speech) inflames men to virtue and to notorious deeds of evil It teaches the wretched how to seek for help It has restored spirit to the timid, con trol to the impeutous, skill to the idle calm to the angered, solace to the un happy hope to the despairing—in short, it has virtually restored life But if we may now turn our argument from the perceptible world to the world of the spirit and hold in abeyance the words of naturalists, we have the oppor tunity of asserting the opinions of Theologians about speech and words. I shall say that so great is the nobility of speech and words that the son him self of God wanted a term named, and that in a single sound IEHI, IEHI that is to say Let there be let there be In amazing fashion he created the amazing and marvelous machine that is the entire world, as well as the almost countless species of things in it Indeed, after the fall of our first parent Adam when this voice had been uttered— Where oh where are you Adam?"—he instilled a great fear in him, as the Scripture testifies from the third chapter of Genesis. There we read I have heard your voice oh Lord, and I was afraid" Further in chapter 17 of Matthew in the New Testament, when the boat of the disciples wa being tossed about by enor mous waves because of contrary winds and a severe storm at sea, and our Savior walked on the waters, the spirit of the disciples, being in dire straits nd filled with fear was raised and strengthened by speech. For as soon as Christ spoke thi speech for their ears— Have faith I am He do not fear"—suddenly the trembling wa driven in rout from their hearts and they all recovered Likewise (again in Matthew 17) the trembling disciplies were comforted when Christ uttered these words Up, let us go from here, (nd) do not be afraid. What more The sacred scriptures proclaim that thanks to speech, oice[2] was restored by Christ and the Apostles to the mute hear ing t the deaf sight *to the blind*, health to the sick life to the dead, and countless other miracles were *performed*. In sum, the voice of the Lord is in irtue and the voice of the Lord is in magnificence

To this day from the time of the Apostles and their successors, speech has made the shining light of the Christian *religion flash forth*—not only in our own lands, but in the remotest region of this great world the bril liance f the Faith has increased, the darkness of wrong has been routed, th disgrace of the cross has been done away with, the sacred and holy Evangel of Christ has been preached, heresies have been destroyed and heretics completely laid low By means of speech the thanks due to God are rendered to Him and sacred prayers are offered up In our actions we ask for heavenly help and in our difficulties we implore consolation and alleviation from God. By speech will this universe one day be destroyed, when the heavens disintegrate in heat when the son of God appears in the clouds, the

The next tw l words re extremely unclear in the microfilm. Despit ur best effort w ca make no satisfactory sense of the Lati which here subj l *Patre* genitus.

This i good example of the semantic problem ca sed by Casserius use of *vox* for both speech and oice In the Latin, both word (i.e., *voce vocem*) are the same

CHAPTER II

On the various designations of the term Larynx and on synonyms for the indicated part

In my proposal to examine the anatomy of the Larynx, the true and genuine *instrument of voice I shall pursue the subject matter uninterrupted* and without any ambiguity That I however may be able in the course of my treatise to move about more conveniently and that the reader may more easily understand what will be set forth about this organ in my fine yet difficult explanations, I shall first consider in review the various designations of Larynx as well as whatever other names the organ of voice has been allotted Thereupon girding myself for the definition of my actual subject I shall very clearly summarize its essence and all my diligent research which can bring to bear on understanding it To facilitate learning and understanding this summary—as, I suspect will presently be clear—will not come in the position in which a good number of anatomists usually put it in setting forth their history of the parts of the body namely when they switch the discussion from the parts of the body to its total structure For I proceed by the opposite and as it were free method from the whole to the parts The Nostrates [sic][1] then along with the Greeks recognize the head of the *harsh wind pipe [trachea] by the name larynx or larynga Aristotle on the* contrary for some inexplicable reason understood the head of the wind pipe by this name Galen in the seventh book chapters one and three of *De usu partium* at one point (and here he incorrectly appropriates this term) gives the name *larynx* to that *little* part which lies between *the pharynx and the* harsh wind pipe [2] at another point (and here he is more correct and accurate) he means by larynx that part which is separated and distinct from the pharynx proper and the other indicated parts On this matter see Galen in his book *De musculorum dissectione* chapter 15 as well as *Book I* chapter 3 of *De motu musculorum* There are some who identify the head of the wind pipe and the organ of breathing and the knot of the throat [prominentia laryngea] with the larynx Even if you should read many authors, these are the meanings given to the term larynx among them We however believe with Galen that the head of the trachea is designated by this term Now just as we find varied meanings for the term larynx so there are varied

Ca seri w probabl referri g t th f ll w ra f Erasi trat f Ceos the f m Al x ndri nat mi t

On th ba i of th cited pa sage i G l (VII I, III) we f ll t und rst d Ca seri bjection th t G l I mi l g th term

names assigned to that part which we are calling larynx. For example, in the Canon of Avicenna and Averroes it is called the head of the lung, which, in the latin idiom Augena attributes to the Arabic. I pass by in silence the invention of Hali Abbas as utterly incompetent and strange—he calls it the collarbone This term, collar-bone should, I think, be rejected as excessively vague common to several parts yet also more suitable to others, and incorrectly appropriated by Hali Abbas. Nor do I add the name epiglottis to the list of other names for this part, although that would agree with the views of certain people My reason is that the etymology of the term shows it to be clearly misleading and inappropriate it is made up of the prepositional prefix epi (meaning *upon* or *above*) and the noun glossa (meaning tongue) which is spelled glotta in the Attic dialect Hence the term epiglottis can designate nothing except some kind of tonguelike covering, as will become more clear in what follows. That term however which the admittedly great scholar Hesychius used I gladly add to my list of other terms he named the part in question the esophagus

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Ca seri w prol bl ref rri g t th f ll w rs f Lra trati f Gei s th f m a Ale ndri anat mi t

On th ba i of th lted p sage i G le (VII I, III) w f ll t d rst d Ca seri bjecti n th t G l n i misu i g th term

worthy of praise than its usefulness. For to this part especially is entrusted the action of the larynx, and voice is formed by it—which is the specific function of this organ In marvelous fashion air passes through and, being compressed, is thrust forth so as to produce voice Hence not without good reason, its inner surface is carefully fashioned, and lightly smeared with some sort of mucosa [tunica mucosa] There is little moisture on it Indeed it is wetter than necessary to the extent that it impedes the formation of voice Because of this there is that well known hoarseness which the catarrh bri gs on

This brings us to its position The part which sticks out and is hump-shaped lies in the anterior position It is, as it were pug nosed and pressed down, and laying claim also to a posterior position for itself touches the esophagus. The upper or higher portion where it lies beneath the epiglottis, looks towards the gullet and little column the lowest part is located above the trachea, as though it were its head, and is like the musical instrument which flute players use In that way trumpets (commonly called trombones) curved and straight horns, in short all wind instruments like pipes and others of that sort, have a head. Just as we produce the most perfect sound relaying on this skillfully crafted instrument, so nature emits, by means of that head, voice which is highly sonorous and thoroughly pleasing to the ears. From this description of its location, the complex of the larynx is, I suspect, sufficiently clear and obvious its connection to the cartilages, with the harsh wind-pipe with the binding of both the special and the common muscles, with the esophagus, with the thorax, with the hyoid and with *the* higher parts with the brain, the help of the nerves, with the heart and aid of the arteries. These comments shall suffice for the establishing of those parts because of wich w have called the larynx th first and proper organ of modulating voice as well as for the brief description of its components *The* body f the larynx, then, is joined together from a simple union of its parts, not from any change in them as a result the larynx has no other *constitu-tion* than its parts, nor any other consequents or differing accidents.[1]

I intend to leave for the proper place a more extensive treatment of these matters, so now I gird myself for an explanation of the parts, first which make up the larynx and, second with by which it has been provided for the modulation of voice And although the *natural* order prescribes that the former should be discussed bef re the latter still the arrangement of the plates demands that we abandon and *change* this order and treat first of the muscles, then of the nerves

1 sing consequences (*consequentia*) nd accidents (*accidentia*) Casserius refers t philosophical notions of primary nd secondary purposes.

CHAPTER III

On the Definition of the Larynx

After I have reviewed the various names of that part with which my dissertation is concerned and since the ambiguity of the part most closely corresponding to it has been removed I offer the following definition of the Larynx It is the organ which consists of the cartilages [cartilagines laryngis] extending the glottis [rima glottidis] and of its membranes—an organ endowed with muscles and nerves, first and foremost constructed to produce voice I said first and foremost" having speech in mind on the authority of Galen for these are his very words in Book 7 chapter 10 of his *De usu partium* where he distinguishes the larynx from the thorax For although the thorax [pulmo] provides the material of voice it will justifiably be considered as the secondary instrument of it Here and there in several places, he also called it an organ For since that which causes some action is an organ in Galen s opinion this term in particular is appropriate yet if it causes the formation of voice, no one will deny that it is an action However since every organ is a body yet certain parts of bodies are soft or hard *some rare or dense, others thick or slight I claim that the body of the* larynx is hard, dense and thick I do this on the grounds that cartilaginous bodies are worked into its make-up In like manner the larynx is large and ample consisting of the three dimensions of length, width and depth there is also a certain protuberance [prominentia laryngea] on it which in men is very conspicuous, but rarely so in women The reason for the variety of the larynx is, according to the opinion of certain individuals, due to the composition of this protuberance—because certain gland like [glandula laryngeae] bodies which are almost coterminous with the larynx, in filling up any hollow or empty spaces, make the chamber equal in women The shape of the larynx is round and circular with however a certain slanting quality to it In its anterior portion it is absolutely circular but in the posterior part from which it faces the esophagus, it gradually changes from a perfectly *circular shape and attains some length Therefore this part* because of its structural outline, is likened to a vessel called the *arytaene*[1] [cartilago arytenoidea] but with a spout with which we pour water for those who would wash their hands Moreover a shape of this sort is not without its advantages, since it is crisscrossed with passages and apertures For there is within the body of the larynx an aperture which is called the little cleft [rima glottidis] fissure or rent of the larynx or glottis Its grace is no less

[1] A Greek word which means "pitcher"

for the present I have set myself the task of examining only the muscles of the larynx) The remaining two [musculi thyrohyoidei], which verge considerably to the side emerge from almost the entire lower border of the hyoid. This is the case in man, but in other living things (especially quadrupeds) the situation is different for in the middle of their passage, the muscles are united, at the bottom, they are divided and split in two Therefore we can rightly call them two-horned or two-footed because they consist of two legs. Of these one part is fixed in the shield shape [cartilago thyroidea], the other in the hyoid bone—and that most conspicuously In origin they are fleshy broad, very close to the internal sides, and continuous. And this is how they lie advancing gradually from their place of origin with straight-down fibers, they settle finally in the same lower part of the first cartilage opposite which are the muscles which precede these and are firmly fixed and exactly the same insertion is preserved. Galen, Vesalius, Fuchsius and Realdus add other muscles to the four already mentioned. But whether they should be considered one, as did Columbus, or even two, as did Galen Vesalius and Fuchsius, observation itself makes unclear Forced by the certainty of what I see however I agree with Realdus in this matter namely that it is only one[3] But I differ from him as well as from the rest, in that I believe that although it bur ts forth from the hield shape it should in no way be considered among the common laryngeal muscles. For if nature had shaped this muscle only for the sake of the larynx, undoubtedly it would encircle the esophagus only very little otherwise this muscle would greatly hinder rather than aid in the swallowing of food or drink Provident nature would have been bound to enclose the gullet not with this muscle but to extend the gullet from one extremity of the shield-shape to the other keeping the esophagus intact. Let us, therefore prompted by dissection alone say that this muscle serves the larynx neither especially nor by itself but only incid ntally—as its structure and position makes amply *clear* For it originates on both sides of the thyroid, along its entire length which is made up of crosswise fibers in a half circle It then advances to a point where it girds the esophagus in a circle whereby it serves the swallowing of food and drink by a sort of involuntary movement, and also aids the natural faculties in passing down food and drink Moreover while these muscles have movement for the sake of the gullet, the first laryngeal cartilage [cartilago thyroidea], to which it i attached, is necessarily constricted and tightened. Hence it aids the larynx—*not in a primary or inherent way* but by chance and secondarily Therefore, at the suggestion of my observation I conclude that this extra muscle not only cann t be reckoned as one f the common laryngeal muscles, but in fact belongs to them only by ccident. So Galen says, in Chapter 7 of his book on dissection of the instrument of voice "The shield sh ped cartilage in the upper areas is bound

[3] Although pparently not differentiated by Casserius separat muscle, he ppears t be describing the course of *musculus constrictor pharyngis inferior pars thyropharyngea* and *pars cricopharyngea*

CHAPTER IV

On the common muscles of the larynx not including an enumeration of all its muscles

The muscles of the larynx are of two kinds the common [musculi laryngis externi] and the special [musculi laryngis interni] Common" is the name given according to all scholars versed in dissection to those muscles which have their origin outside the larynx but end in it Special is the name given to those muscles which originate from the larynx and in turn have their insertion circumscribed in it I imagine it is accurate enough to think that this nomenclature derives from practical experience and not from any artificial criteria *There is, however no agreement among the authorities on the* number of all the muscles which serve this organ Galen along with Fuchsius and Vesalius (in *De usu partium* VII xi xii and XVII ix) asserts unequivocally that the larynx, as a self-contained structure is moved by twelve muscles but as a structure also of other parts, he claims it is moved by only eight muscles In all then he counts twenty muscles for the larynx Avicenna, on the other hand thinks there are eighteen muscles and there are even some who have not hesitated to enumerate thirty two muscles. It is *certainly not my intention to contradict either Galen or any other skilled* investigators (perhaps they busied themselves more frequently with the dissection of other animals than of man) but I shall maintain fearlessly what I have been allowed to observe in the human larynx—not once but again and again There are then exactly thirteen muscles, of which four are common and the rest special and thus do I reject the opinion of Columbus, who made a claim for fourteen muscles

Taking my beginning from the common muscles, I claim to have observed *that the first two of these [musculi sternothyroidei]* break out from the superior and inner part of the sternum where it juts out in the neck where the first two muscles of the hyoid bone come forth Initially these muscles are membraneous, but widening and then they advance upwards over the anterior region of the harsh wind pipe becoming fleshy and a little broader They continue until flexible as they enter the lowest part of the first[1] thyroid cartilage On their body one can note certain nodes or nerve-like markings called circumscriptions by the Greeks The same thing is visible on the straight abdominal muscles (which I shall consider in the proper place since

[1] The Latin phrase i[illegible] *prima ca[illegible]tilagi[illegible]is Thyroid[illegible]s* [illegible] d theref[illegible]re [illegible] *of th[illegible] first th[illegible]roid* [illegible]rtilag[illegible] but [illegible]tructurally w[illegible] fail t[illegible] [illegible] what Ga[illegible]seri[illegible] mean[illegible] by *p[illegible]im[illegible]* "first"

[illegible] [illegible] [illegible] pp[illegible] [illegible]

CHAPTER V

On the Special Muscles of the Larynx, generally considered, and on the first pair in particular

I believe I have satisfactorily explained those muscles of the larynx called common. Now that I intend to treat the muscles proper of the larynx, I shall describe their number, location and true differences. Authorities vary greatly on the matter of their number: some like Galen, Fuchsius and Vesalius think there are twelve, others, fewer. But I have had the opportunity to observe without prejudice in all animals, (for example cows, horses, pigs, sheep, men) nine muscles in all, as a result of careful dissection of most of these muscles. My drawings make this clear. Even though that small muscle ascribed to the arytenoid possesses two bellies [musculus arytenoideus transversus, musculus arytenoideus obliquus], however unclear, by means of which a distinction seems to make a fifth pair and the muscles are commonly thought to number ten, nevertheless its structure and use clearly testifies to the fact that it is a single muscle. Careful inspection will reveal that this is the truth as far as its structure is concerned. Concerning its use I shall have a thing or two to say in passing. Every muscle performs its specific task through contraction. Therefore if this muscle is a double one set against itself, it will necessarily produce a double and opposite action as long as it moves by contraction, which corresponds to it in principle. Clearly then, when a muscle acts not by a double and contrary movement, but only by a simple movement, there will be only one, not two muscles—unless of course one should believe that the muscle operates contrary to the edicts of nature. But I would not deny that the muscle is tend alike in the middle. This I believe serves the purpose of strengthening it and making it solid so as to prevent its suffering the inconvenience of rupture—a matter worthy of some concern—during its constant movement and agitation with the arytenoid. Hence I am justified in excluding the tenth muscle from the others. Furthermore, of these nine those which make up the first pair are two [musculi cricothyroidei], not four as Vesalius believed (in Chapter 20 of Book II of his great work) and also Sylvius, Fuchsius and several other anatomists. They claim that these muscles regulate the movement of the "shieldshape" along with the cricoid. And Vesalius, an otherwise skilled and especially careful anatomist, places two pair of muscles along either side of the "shieldshape": one pair consist of those which verge to the front [pars recta] and lie on top of each other, the other pair [pars obliqua], of those which, like the intercostal muscles, intersect each other crosswise with fibers. Vesalius believed that the first of these muscles, the exterior ones, had

together by those muscles which encircle the gullet growing out from its [cartilago] uppermost parts. It must be established with certainty that I know that its movement is accidental, not inherent I cannot in truth posit two muscles, as the authors above mentioned do on the basis of my dissections For since it springs forth from the posterior part of the mouth that lies opposite the vertebrae of the neck and runs the smooth and membraneous length of the gullet without interruption it is obvious that one can in no way speak of two muscles Arising from its own full and fleshy origin towards the front, it is fixed in the sides of the thyroid cartilage along their length As a result of my personal observation it is obvious that no division or membraneous line runs along those filaments which could persuade me that one should consider this muscle doubled Therefore it seems that those have good reason to depart from Galen s view who said this muscle was one because it enfolds the esophagus in a circle-like sphincter Galen supposed it was a double muscle one on each side and these are his words in Chapter 2 of his book on dissection of muscles Two other muscles arising one on each side in the posterior extremities of the shield shape are fixed in the gullet and they likewise embrace the gullet like sphinctoral constrictors These bind the cartilage together tightly

Therefore no more than four common laryngeal muscles should be recognized For in my opinion we cannot and should not count the other one among the common laryngeal muscles, as does Vesalius—not even if he shows distinctly that many other muscles arise from the inner part of the hyoid and that individual muscles on either side are fixed in the base of that cartilage which is called the epiglottis. For their function is to raise the epiglottis, the lid of the larynx when it is shut in the swallowing of food or drink to prevent breathing from being restricted Consider this view to be most in harmony with the truth as far as certain animals are concerned in cows, pigs and all quadrupeds it is abundantly clear But in the case of man on applying complete diligence in dissection in no way will it be possible to find such a muscle in the root of the epiglottis, a subject which will be discussed in the proper place

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their origin from the lower part of the shieldshape" and descending obliquely ran to the anterior parts of the larynx and wound their way into the unnamed cartilage [cartilago cricoidea] The other muscles, the interior ones, are situated under these and emerge windingly from the first though in a different way But as elsewhere quite often so in this case too Vesalius was deceived by his extreme diligence for his curiosity concerning both structure and use drove him into error For by reason of construction or rather structure those muscles which he divides into four cannot be counted as *more than two if we are to stick to the truth of the matter But how can we* explain the mistake of so great and distinguished a man? We find this quite easy since the same error frequently happened to us While struggling to separate the extremely thin muscles (of each kind *present*) we were enticed by another mistake to separate a single muscle into two sections as though it were a double muscle and subsequently we believed that there were in actual fact two muscles But that this is mere imagination even in the case of the use of the muscle is clear from the fact that he seems to have attributed movement to the unnamed cartilage yet the actual base [cartilago cricoidea] as it were of the entire larynx completely lacks movement For if *those two muscles are attached according to his thought to the cricoid and* unnamed cartilage [cartilago thyroidea], it is doubtful that they move the cricoid and unnamed cartilage—for obviously the movement of the muscle is contrary to its principle Thus do I dispose of Vesalius opinion on the first pair For observation exposes only two muscles, one on each side which emerge from the lower part of the first cartilage the thyroid, both from the outer and inner part but from the inner part the muscle emerges a little higher Each has a wholly fleshy origin (into which the beginning of the recurrent nerves is, as a matter of fact inserted) and each tends to be broad and is triangular in shape Furthermore these muscles provide from *behind the posterior part with certain fibers descending obliquely* (so that they therefore are given the name of obliquely descending muscle [pars obliqua]) then they pass rapidly to the front towards the cricoid and by pass it Being initially broad they become thin and vice versa Finally they push against the anterior and lateral part of the cricoid according to their various positions, and here they stop being in no part fleshy From the above considerations it is clear that at least these muscles in the front can appropriately be called cricothyroid *(as certain anatomists who delight in* assigning names have decided) But when they do not start from the cricoid in the front and go to the back or go from the lower base of the thyroid, but rather stretch from the thyroid to the cricoid they should more accurately and correctly be called thyro-cricoids Furthermore in animals, as for example in the cow horse and pig in our drawings, one can see it more clearly than they appear in man

CHAPTER VI

On the Second, Third and Fourth Pairs of the Special Laryngeal Muscles

Two other muscles [musculi cricoarytenoidei posteriores] follow these and make up a second pair they seem to be almost completely united and stretched o er the cricoid cartilage at their origin. Contrary to the general belief of all anatomists their origin does not start in the lower part where they make a sharp corner but in the upper part, opposite the joints of tl e un named cartilage and the arytenoid, for there it is quite clear that nerves are implanted. Joined together they emerge from the arytenoid cartilage their composition is fleshy membraneous and rather strong. Advancing from there they keep on separating little by little. Verging down from above they stick closely to a long and straight rough line finally coming together again simultaneously they join each other and grow so large that they everywhere fill up the broad back aspect of the cricoid which lies near the region of the esophagus. On the basis of their configuration and position we get that elegant expression for their shape which looks almost exactly like the cowl monks wear Consequently since Realdus and other anatomists called the muscles of the shoulder-blades monkshoods" as a result of such a shape, we shall be allowed to give the same name to these muscles. Indeed, they look broad and oblong, even thick they are made up of various brightly differentiated types of fibre and they stick to the back of the cricoid, which is ery similar to the breast bone of birds on which lie the so-called pectoral muscles (which put the wings in motion like a glossocomium [a type of pulley system]) Because of this similarity the muscles under discussion can be n med the pectoral, or thoracic muscles Yet if we examine these muscles separat ly when they are divided, outside their natural position and raised up, we shall, to the extent that their shape is very similar to birdwings, with great justification call them the winged muscles. This is consistent with the serious Bauhinus Basiliesis, anatomist and famous botanist, who called them the rear mucles of the cricoid, but not of the cricothyroid. As a matter of fact as dissection shows, ari ing from the arytenoid they are implanted in the cricoid, not the thyroid But this haggling about names is pointless, f r it neithe add nor d tracts anything of substance Therefore I now lea e thi matter and pass on to the remaining muscles. Not far from these muscles which we have already discussed, two smallish muscles can be seen which make up the third pair [musculi cricoarytenoidei laterales]. A large part of them lies under the monkshoods They have a fleshy soft and sharp origin, and do not arise from the side of the cricothyroid, as certain

their origin from the lower part of the shieldshape and descending obliquely ran to the anterior parts of the larynx and wound their way into the *unnamed cartilage [cartilago cricoidea]* The other muscles, the interior ones, are situated under these and emerge windingly from the first though in a different way But as elsewhere quite often so in this case too Vesalius was *deceived by his* extreme diligence for his curiosity concerning both structure and use drove him into error For by reason of construction or rather structure, those muscles which he divides into four cannot be counted as more than two, if we are to stick to the truth of the matter But how can we explain the mistake of so great and distinguished a man? We find this quite easy since the same error frequently happened to us. While struggling to separate the extremely thin muscles (of each kind present) we were enticed by another mistake to separate a single muscle into two sections as though it were a double muscle and subsequently we believed that there were in actual fact two muscles. But that this is mere imagination even in the case of the use of the muscle is clear from the fact that he seems to have attributed movement to the unnamed cartilage yet the actual base [cartilago cricoidea] as it were of the entire larynx completely lacks movement For if those two muscles are attached according to his thought to the cricoid and unnamed cartilage [cartilago thyroidea], it is doubtful that they move the cricoid and unnamed cartilage—for obviously the movement of the muscle is contrary to its principle Thus do I dispose of Vesalius opinion on the first pair For observation exposes only two muscles, one on each side which emerge from the lower part of the first cartilage the thyroid, both from the outer and inner part but from the inner part the muscle emerges a little higher Each has a wholly fleshy origin (into which the beginning of the recurrent nerves is, as a matter of fact inserted) and each tends to be broad and is triangular in shape Furthermore these muscles provide from *behind the posterior part with certain fibers descending obliquely (so that* they therefore are given the name of obliquely descending muscle [pars obliqua]) then they pass rapidly to the front towards the cricoid and by *pass it Being initially broad* they become *thin and vice versa* Finally they push against the anterior and lateral part of the cricoid according to their various positions, and here they stop being in no part fleshy From the above *considerations it is clear that at* least these muscles in the front can appropriately be called cricothyroid (as certain anatomists who delight in assigning names have decided) But when they do not start from the cricoid *in the front and go to the back or go from the* lower base of the thyroid but rather stretch from the thyroid to the cricoid they should more accurately and correctly be called thyro-cricoids Furthermore in animals, as for example *in the cow horse and pig in our drawings*, one can see it more clearly than they appear in man

CHAPTER VII

On the Muscle of the Larynx Which Lacks a Mate

There remains the final muscle to describe. In this case it would seem especially worthwhile to consider whether this muscle should be thought of as a single or a twofold muscle [musculus arytenoideus]. Although Vesalius and Fu hsius are unanimous in reporting that there are two muscles, I agree with Realdus Columbus that it is only one. Unless I am mistaken the reason for their erro was the peculiar shape of this muscle. For it displays two fleshy bellies and in the middle it is like a sort of thin tendon and membraneous but the bellies gather them together and join them a little more tightly so that it gives the false impression of being a double muscle. However along with Columbus I have never been truly convinced that this fleshy mass, in man as well as in animals, consists of two muscles. The course which this muscle runs is as follow. It starts from the last root [facies posterior processus muscularis] of the one part of the arytenoid, does not arise from the length of this cartilage and after the fibres have crossed over transversely returns on a sudden to its starting point, and ends at the base of the same cartilage.[1] In the m ke-up of its fibres this muscle hardly differs from any of the common muscles, where they are attached to the opening. Furthermore at its point of origin and beginning, it is seen t be fleshy membraneous and to a certain degree pointed from this point it approaches *the* middle of the cartilage transversely and proceeds while (growing) a bit more fleshy and thick after losing this thickness it swells into a belly. But you will not find it ending completely in this belly for immediately after this line it uddenly stretches further becoming broader and forming a sec nd belly similar t the first. Then, returning to its origin, it finally ends in the middle of that cartilage from which it started. This examination concerning the course of this muscle could well raise the question why for example it is so unequal and multiform now thick, now thin then changing from one belly into two and back again into one *from* two. We should not bother with thi sort of inquiry on the grounds that it i foreign to our treatm nt, fo ou intention at this p int is to discuss structure not purposes,

[1] Caseri properly observed that the *m. arytenoid* us is composed of both horizontal ad blique fibers; he did not, however disti guish between t separat bundles of fibers (*m arytenoideus transversus* nd *m aryt noideus obliquus*). With this perspective, the *m arytenoideus* would ppear t the dissector t take on the shape of "bow tie (See second facsimil diagram *T bul XIII Secunda Hominis*, letter E" of XII, XIII XV.)

The mea ng i nclear the word *opeal* g" l translation of the Lati lord Greek stomache.

anatomists believe but from the arytenoid lying rather along its side for the sake of the insertion of the nerves hence they *are called the muscles of the arytenothyroid or lateral muscles.* From there they are carried forward a bit and become larger thicker and more teeming with flesh then they fall towards first the inner then the outer sides. At last without changing their fleshy substance they take on a thinner and more narrow pyramidal shape before disappearing into the ring like cartilage. To these oblique muscles *has* been entrusted the function of gently relaxing and contracting the fissure along the side (as will be evident in the proper place) After these two other muscles make up the fourth pair which link the first cartilage to the third [musculi thyroarytenoidei] These are marked by a numerous variety of different fibres straight oblique rising and descending Indeed to one skilled in anatomy even they could seem more numerous. Consequently not a few anatomists have been deceived by this variety and described more muscles than is reasonable It is no surprise that certain anatomists have through inaccurate examination of the structure, even made the mistake of believing that the small upper portion of this muscle rises all the way to the base of the epiglottis This portion makes the movement which is the opposite of that made by the muscle [ligamentum hyoepiglotticum] which comes from the hyoid bone and is attached to the upper base of the epiglottis to raise it—hence it is given the name of opponent Thus four muscles are assigned to move the epiglottis—and one can hardly conceive of a more ridiculous notion since no portion of this muscle touches the epiglottis. So *great then is the diversity of fibres in these muscles that unless a person brings to bear his keenest eyesight he will easily fall into error* So *great* is their unity that he who delights in the discovery of new muscles can easily persuade himself into imagining that he has in fact discovered new muscles. A similar variety of fibres appears in the deltoid muscle [musculus deltoideus] which pulls the shoulder towards the chest and also in that very thick *muscle [musculus rectus femoris]* which by contracting moves one femur above the other femur That entire mass, then consists of at least two muscles, one on each side and not of more These muscles are at their origin broad fleshy continuous in turn fibrous they lie in the inner and snub-nosed middle region of the shieldshape and they run along almost its entire length by no single principle *This is evident in cows because of the* enormous size of those muscles in them their numerous fibrous delineations appear distinctly Gradually descending from that place as they advance posteriorly they keep growing more *narrow until they are implanted along* and in the side of the arytenoid *These parts of the* arytenoid constrict narrow and squeeze shut the fissure in the forward part [as a result of contraction by the thyroarytenoid muscle]

CHAPTER VII

On the Muscle of the Larynx Which Lacks a Mate

There remains the final muscle to describe In this case it would seem especially worthwhile to consider whether this muscle should be thought of as a single or a twofold muscle [musculus arytenoideu] Although Vesalius and Fuchsius are unanimous in reporting that there are two muscles, I agree with Realdus Columbus that it is only one Unless I am mistaken the reason for their error was the peculiar shape of this muscle For it displays two fleshy bellies and in the middle it is like a sort of thin tendon and mem branceous but the bellies gather them together and join them a little more tightly so that it gives the false impression of being a double muscle How ever along with Columbus I have never been truly convinced that this fleshy mass, in man as well as in animals, consists of two muscles. The course which this muscle runs is as follow It starts from the last root [facies posterior processus muscularis] of the *one* part of the arytenoid, does not arise from th length of this cartilage and after the fibres have crossed over transversely returns on a sudden to its starting point and ends at the base of the same cartilage In the make up of its fibres this muscle hardly differs from any f the common muscles, where they are attached to the opening. Furthermore at its point of origin and beginning, it is seen to be fleshy membraneous and to a certain degree pointed from this point it *approaches* the middle of the cartilage transversely and proceeds while (growing) a bit more fleshy and thick after losing this thickness it swells into a belly But *you will not find* it ending completely in this belly for immediately after this line it suddenly stretches further becoming *broader* and forming a second belly similar to the first. Then, returning to its origin, it finally ends in the middle of that cartilage from which it started This examination con cerning the course of thi muscle could well raise the question why for example it is so unequal and multiform now thick, now thin then chang ing from one belly into two and back again into one from two We should not bother with this sort of *inquiry* on the grounds that it is foreign to our tre tment, for our intention at this point is to discuss structure not purposes,

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The meaning [illegible] the word [illegible] translation f th Latinized Greek [illegible]

Since however his scruple might disturb somebody I shall offer a rather simple explanation to avoid keeping anyone in suspense any longer For the muscle under discussion is naturally so constituted for the same reason that several other muscles appropriate two bellies The muscle which moves the lower jaw downwards [musculus digastricus] and also that oblong muscle [musculus omohyoideus] which comes from the shoulder blade to the hyoid bone are both provided with two bellies Thus they are made stronger by their own tendon from whose intermediate position the bellies are formed and resist more vigorously the powerful motion of the jugular artery (carotid) For if they had been completely of fleshy substance nature would have displayed too little concern for them The same reason applies to the two bellies of our muscle For since the little fissure which the third cartilage makes, constantly moves the muscles about the middle by dilation and contraction and stirs them in its marvelous way the muscle has been made of tendons and flesh in order to resist (especially during suspension of breathing) those violent movements and avoid splitting And to prevent this muscle from being in the way due to too large a mass or the movement of that cartilage nature in her full wisdom has made it quite small For so small is the muscle that it is considered the tiniest of all the muscles in the entire body And when it constricts the larynx with might, it opposes the action of many muscles—which seems indeed a thing of wonder

It displays a semi-circular shape This shape is the true structure and description of the laryngeal muscles this is their true number They are in my opinion fixed at thirteen not fourteen (as Realdus and Fallopius claimed) not twenty (as Vesalius believed) and not eighteen (as Fuchsius said) Of these thirteen there are four pairs of laryngeal muscles proper a single muscle without a mate (hence the term unwedded) and two pairs of common muscles.

CHAPTER VIII

On the Recurrent Nerves

Now that I have completed the investigation of the laryngeal muscles, my enthusiasm demands that I take up in my discussion a description of the nerves which impart to the muscles the ability to move. In my description of these nerves, drawi gs f great clarity shall reveal nature's enormous skill, the industry of the great Artificer and also a virtually incredible piece of handiwork. For the nerves have been constructed by the benign parent of ll things, God and Nature in so marvellous a fashion that I cannot fail to be astounded at the many rash judges who did not blush at accusing the second one the mother of all things, of a want in skill and at calling her a step-mother. For a man of dullest intellect will be able to ascertain her forethought and cleverness. These nerves run as follows some wind along transversely some obliquely some downwards after starting upward and vice versa, some to the left, others to the right, and finally enter the muscles. And the reason? They run by such a varied course because of the position of the muscles which they pass under. For the nerves cannot be inserted to any part of a muscle but either to its head alone, or its middle (commonly called the belly) but below the middle for example at the end or tendon they can never be implanted, since on contraction of the fibres the beginning of the muscles would approach the condition of the end. For all muscles are constantly contracted towards their origin provided that they are supplied with shoots of nerves. Since then, only one insertion or the other of the nerves l to the muscles is possible it was necessary for them to run in so aried a fashion. Anatomy teaches that some of the muscles have a transverse position, more have an oblique position, the rest a straight position according to whether they look up from below or down from above. Two nerves [nervus laryngeus superior], looking down from above, wind into two laryngeal muscles [musculi cricothyroidei] by way of two offshoots. One of these utgrowths, stret hing towards the broade part of the thyroid (shield shape) cartilage is attached to it the other one runs along the oblique muscles and those muscles which are stretched to the pectoral bone. Just a these two muscles [musculi cricothyroidei] descend from above, so also the two nerves which advance to the position of the muscles are formed for their sake. Just as the muscles which look upwards from below [musculi sternothyroidei] are set over against the former muscles, so it was necessary for the nerves to be channeled from the lower parts to the upper. Since, however all the nerves emerge from the neck or the spinal medulla, it will be pertinent to inquire first from what beginning the nerves that are scattered throughout the larynx take their origin, and secondly how they are implanted into the muscles. It is not reasonable for them to proceed from

the neck or the cervical spinal medulla since then they would be destined to be oblique And even if this objection is removed, still it would be reasonable for nature to share the nerves not from the most worthless origin of the nerves, but from their more worthy one namely the larynx which is the chief organ of voice Therefore consider the brain The nerves which originate in the brain emerge from two mutually distinct and separate sources, inasmuch as they come from the sixth [N IX X XI] or seventh [N XII] pairs From those of the seventh pair they could not possibly spread forth since they would be completely useless, being as it were oblique Therefore, clearly they come from those nerves of the sixth pair These nerves run straight down through the neck along either side of the trachea and advancing a little from their point of emergence they immediately scat ter into many branches. Some of them creep to the chest heart lung stom ach others go further and advance to the belly liver spleen and almost all the parts contained in the abdomen Indeed since they cannot stretch from the *straight advance of the nerves from above to the lowest parts, to the* laryngeal muscles either laterally or obliquely nature the doer in her cleverness and amazing foresight discovered a most suitable aid for the requisite action From the nerves which continue on to the chest she makes a double branch one on each side return by the same path they went down Of these the right branch, being higher than its mate is supported and enfolded by that branch [arteria subclavia] of the great artery [truncus brachiocephalicus] which proceeds to the right arm The left one being much lower than the former winds around the trunk of the greatest artery [arcus aortae] where it curves back and descends then bending back slightly it suddenly creeps upwards along the same path winding skillfully into the inferior muscles of the larynx Similarly in the case of drawing off water from its source by canals, (man s) art separates them off to the sides, *up down in front behind obliquely* or hither and thither through ascent and descent Moreover when the nerves are moved towards their origin which they *take from the brain or the beginning of the medulla* a contrac tion toward the lower parts, near the trunk of the large artery will take place through motion of the recurrent nerves which are inserted into the lowest muscles of the larynx When the nerves from which branch those notable offshoots in *remarkable looping are moved a pulling from below* upward to the head will take place When near the head contrary motions of the sixth pair and the recurrent (nerves) succeed each other that move- ment is neatly represented as corresponding to metaleptic or transumptive motion Metaleptic motion is that which mechanical *laborers*, as well as the doctors named organici employ in the instrument which is properly called *glossicomium*[1] By means of this instrument doctors restore with the great

[1] Ca seri f ll w G l (3 73) i *comp ri g th recurre t* rve to cord stretched round the p ll y f the gl ssicomi m (argl l ppll nce sed t set broken limb) by th met leptic cti n (alt rnati g m m t) the muscles re adj sted f ice prod cti n

est ease and calm, people whose legs and arms run riot to their former place. The construction of this machine is as follows. Its top and bottom sections contain a plank, and on the machine several little pulleys are built up; to these pulleys is tied in criss-cross fashion a series of snoods. Now when doctors plan to use it, for example, to reset dislocated bones, they encircle the broken limbs with ropes that hang down from the *glossocomium* and by a gentl[e] tightening of the ropes a tension in either direction, up and down, is effected, which is suitable and correct for the affected limbs. In these movements lies what we are calling metaleptic motion. Hence it is clear that metaleptic motion consists of raising and lowering, whether in elevation or depression, and of contrary but simultaneous, motions of the same thing. Our mind hasn't the power even to conceive that this motion can be effected without the pulleys. Therefore Avicenna rightly denied that the motion of ascent and descent, arising at one and the same time in one situation, could take place unless there should be present something resembling the *gyrgillus* above which the revolving and circling is carried on. *Gyrgillus* is the proper designation for the little wheel, or instrument, by means of which spinning women roll up their thread, and it is perhaps so called fr[o]m the fact that it spins around. Quite similar is the *trochlea* (type of pulley system) or *orbiculus striatus* (disk) made of wood or bronze by means of which water is scooped from a well as a connecting rope is lowered and raised. But now we must elucidate more thoroughly the system of recurrent nerves and reveal more abundantly the power, wisdom and providence of the Great Artificer (to which Galen bears brilliant and marvellous testimony in the seventh book, chapter 14, of *De Usu Partium*); therefore it is fitting to compare to this artificial transumptive motion the motion of the recurrent nerves by which they are moved towards their first origin. Is it not the case that in artificial *metaleptic motion* the origin of motion starts around the axl[e] of the instrument known as *Glossocomium*? Further, that the supports or appendices of the net are stretched all the way to the pulleys. For a noose is most suitable for this purpose—that is, a noose which consists of two appendices. Indeed, at least some older writers called it The Wolf, perhaps because it had four limbs (supports). Is it not possible to see the same thing in the movement [o]f the so-called recurrent nerves while they are being moved from their own origin. Instead or the plank there is the brain, from which the nerves come *forth* and the nerves are *like the noose*. Furthermore, as in the case of that pulley along which the noose curves as it is twisted into a spiral, dosen't it play the same role as the artery around which the nerves are twisted? For this reason it is called the turning post, or *k[a]mpter* in Greek. In the cow and horse the shield-shape is like the pulley and at its upper tip some offshoots of the recurrent nerves are seen to come out through certain sculpted apertures.[1] Consider also that where the recur

[1] That branch of the recurrent nerv[e] (which we distinguish today as the N. *laryngeus superior*) enters the shield-shape (*cartilago thyroidea*) [a]t [the] second metalept[ic] point [o]f the machine.

the neck or the cervical spinal medulla since then they would be destined to be oblique And even if this objection is removed, still it would be reasonable *for nature to share the nerves not from the most worthless* origin of the nerves, but from their more worthy one namely the larynx, which is the chief organ of voice Therefore consider the brain The nerves which originate in the brain emerge from two mutually distinct and separate sources, inasmuch as they come from the sixth [N IX X XI] or seventh [N XII] pairs From those of the seventh pair they could not possibly spread forth since they would be completely useless, being as it were oblique Therefore clearly they come from those nerves of the sixth pair These nerves run straight down through the neck along either side of the trachea, and advancing a little from their point of emergence they immediately scatter into *many branches Some of them creep to the chest, heart lung, stom*ach others go further and advance to the belly liver spleen and almost all the parts contained in the abdomen Indeed since they cannot stretch from the straight advance of the nerves from above to the lowest parts, to the laryngeal muscles either laterally or obliquely nature the doer in her cleverness and amazing foresight discovered a most suitable aid for the requisite action From the nerves which continue on to the chest she makes a double branch, one on each side return by the same path they went down Of these the right branch being higher than its mate is supported and enfolded by that branch [arteria subclavia] of the great artery [truncus *brachiocephalicus*] which *proceeds to the right arm The left one* being much lower than the former winds around the trunk of the greatest artery [arcus aortae] where it curves back and descends then bending back slightly it suddenly creeps upwards along the same path winding skillfully into the inferior muscles of the larynx Similarly in the case of drawing off water from its source by canals, (man s) art separates them off to the sides, up down in front behind obliquely or hither and thither through ascent and descent Moreover when *the nerves* are moved *towards their origin* which they take from the brain or the beginning of the medulla a contraction toward the lower parts, near the trunk of the large artery will take *place through motion of the recurrent* nerves which are inserted into the lowest muscles of the larynx When the nerves from which branch those notable offshoots in remarkable looping are moved a pulling from below upward to the head will take place When near the head contrary motions of the sixth pair and the recurrent (nerves) succeed each other that movement is neatly represented as corresponding to metaleptic or transumptive motion Metaleptic motion is that which mechanical laborers, as well as the *doctors named organici* employ in th instrument which is properly called *glossicomium* [1] By means of this in trum nt, doct rs r st re with the great

[1] Ca serlu f ll w G l (3 73) in comp ri g th rec rre t nerves t cord stret hed *round th pull ys f the gl ssicomi m* (rgical ppli nce sed t set brok n limb) b th i metalepti cti n (lt rn ti g m vement) th m scl re dj sted f lee prod cti

or two fingers squeeze them, the voice is lessened If the nerves are tied or split, the voice is not only lessened, but completely disappears If they are cut off the animal will continue on through life mute But if they are first tied and then undone again the tone of these nerves returns and is one and the same for all other nerves, in as much as they take on the appearance of the constituent nerves. It should, however be observed that they differ considerably in quality according by degrees some are more moist than others, some dryer some softer and some harder Furthermore they are everywhere of consistent constituency for example the trunks of the nerves are like the substance of their origins. So the nerves of the brain (which consists of three parts—two membranes and a medullary body) and also of the larynx resemble in substance their trunks, and therefore the origins of their trunks. They are quite small and slight so that they deceptively escape our eyes. The quantity of muscles, however in which they are inserted demanded such nerves, for the nerves must necessarily correspond in a certain proportion to those muscles. Yet their number is not infinite, if indeed (in Galen) the two recursive nerves are made up of the nerves which ascend to the larynx these two emerge from two branches of the sixth pair of nerves that start closest from the brain Their shape to be once more repetitive is curved backwards and ring like so that they are called reflexive recurrent and recursive The connection is obvious from what I have said.

rent nerves ascend the artery is firm stable and smooth not rough, unequal or moveable that it sits not just anywhere but in a due and proper place just as the pulleys which being firm stable and smooth not rough or unequal fittingly have been placed not just anywhere but in a fixed determined and most suitable place For so they ought to have been constructed and shaped Consequently neither the clavicles nor the bones or ribs or anything else of the chest s multitudinous content could be suitable for discharging such a function For although there are some of them which are firm not rough and not unequal these are not at all situated in a place suitable for nerves rather they lie on the external part which is full of danger and from which nerves shy away strongly And that for a simple reason *being exposed to harm those very delicate bodies would be removed* from nature s right state and position Therefore since nerves must shoot off far and wide to all the muscles of the entire body in order to provide them with motion and sensitivity *and since just as the soul is directed* through their agency as a horse is by reins and bridle so it could at will move and pull hither and thither the most distant parts of the body—(because of this) nerves advance flowingly obliquely transversely and by varied and multiform steps for their greater safety And the further nerves are from their point of origin and branching the more is their strength increased For since the origins of nerves are quite moist and soft the closer they are to the brain their prodigal source the more moist and soft and hence weaker is the nature which they acquire On the other hand the farther they are from the brain the more they grow dry and hard, and thus become stronger Indeed the warmer the places and paths are which they pass through the greater is the dryness and hardness which they take on and the greater the strength which accrues to them Thus the artery and heart impart much dryness and hardness *to them Everyone realizes how* much usefulness and suitability is imparted to the nerves as they advance further and also how much protection and safety there is for the recurrent *nerves because they are rather distant from their beginning*

But let me now return to the point where the digression began In transumptive motion the noose was adapted to the pulley around which it runs, and a limb properly attached to the extensions of the noose undergoes opposite motions at one and the same time one section being pulled up and the other down so in natural motion the nerves which being attached to and resting on the artery they turn around are inserted into the muscle sustain an up and downward motion at one and the same time For this reason Galen in the fourth (book) sixth chapter of *De Loc Affect* calls them current or recurrent and recursive because like horses on the fields they run back and forth Because of this motion they *are called regressive* by Avicenna But they *also deserve to be called the vocal nerves since they provide* the ability and breath necessary to modulate the voice If anybody *should doubt this*, he should handle these nerves in various ways in his hands Then he would observe that various differences of pitch arise If one

or two fingers squeeze them, the voice is lessened If the nerves are tied or split, the voice is not only lessened, but completely disappears If they are cut off the animal will continue on through life mute But if they are first tied and then undone again the tone of these nerves returns and is one and the same for all other nerves, in as much as they take on the appearance of the constituent nerves. It should, however be observed that they differ considerably in quality according by degrees some are more moist than others, some dryer some softer and some harder Furthermore they are everywhere of consistent constituency for example the trunks of the nerves are like the substance of their origins. So the nerves of the brain (which consists of three parts—two membranes and a medullary body) and also of the larynx resemble in substance their trunks, and therefore the origins of their trunks. They are quite small and slight so that they deceptively escape our eyes. The quantity of muscles, however in which they are inserted demanded such nerves, for the nerves must necessarily correspond in a certain proportion to those muscles. Yet their number is not infinite, if indeed (in Galen) the two recursive nerves are made up of the nerves which ascend to the larynx these two emerge from two branches of the sixth pair of nerves that start closest from the brain. Their shape to be once more repetitive is curved backwards and ring like, so that they are called reflexive recurrent and recursive The connection is obvious from what I have said.

TABVLA PRIMA ❋ PRIMAE HOMINIS

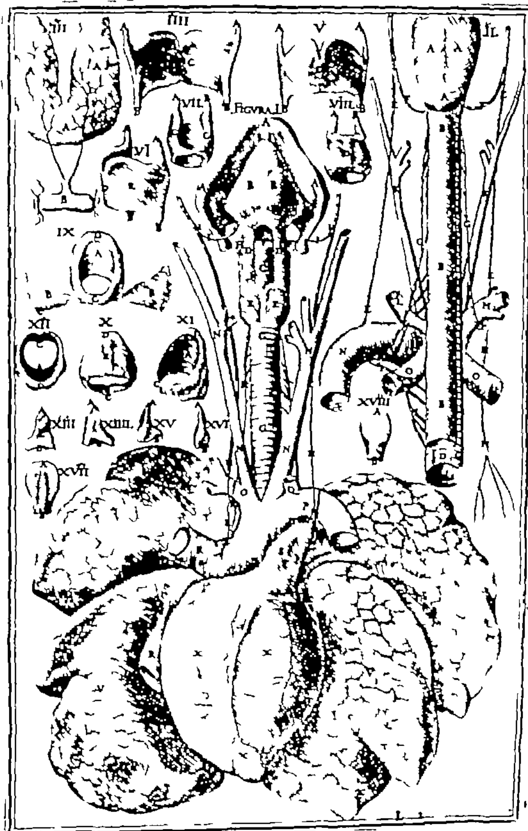


Facsimile f th First An t mical Di gram.

TABVLA XIII ❋ SECVNDA HOMINIS 69



Facsimile of the Second Anatomical Diagram.



F csimil of th Third Anat mical Diagram

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S U P P L E M E N T U M 260

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SUPPLEMENTUM 269

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SUPPLEMENTUM 260

BACTERIOLOGICAL STUDIES ON EXUDATIVE OTITIS MEDIA OCCURRING IN SIX COMMUNITIES OF ALASKAN NATIVES

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To the memory of

JARL AXEL E. GRÖNROOS M.D

A warm friend and a brilliant intellect —
deeply missed

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INTRODUCTION

Acute chronic and recurrent suppurative otitis media have long been recognized as major health problems of the aboriginal people of Alaska, particularly those living in the isolated village environment out of reach of prompt medical attention. It was not until completion of a survey conducted in 1956 by consultants to the Alaska Department of Health, under the sponsorship of the U.S. Children's Bureau, that a statistical appraisal was made of the epidemiological and clinical magnitude of this problem (1, 2). A total of 899 individuals was examined, 84% under 20 years of age. Of the Eskimos examined, 33% had significant hearing loss and 57.9% had lesions of the tympanic membrane. Among Indian subjects, 23.3% had significant hearing loss and 43.6% had lesions of the tympanum such as perforation, scarring, retraction or inflammation due to previous or existing otitis media. Mastoidectomy was recommended urgently for 3.9% of all the subjects examined. Prophylactic removal of tonsils and adenoids was recommended for 41.2% of the children examined with view of reducing the prevalence of otitis and mastoiditis. The survey team estimated that among the children and youth of the Eskimo population alone 739 persons (3.74%) were in need of mastoidectomy and that prophylactic removal of tonsils and adenoids might be indicated for 2785 persons (14.1%).

Following the 1956 survey, the Alaska Department of Health and Welfare with the assistance of the U.S. Children's Bureau, conducted a study aimed at demonstrating ways of reducing the prevalence of acute and chronic otitis media. This was carried out in six villages in the Yukon-Kuskokwim delta region, between September 1957 and September 1959. The study demonstrated, when analyzed and summarized (3), that the aggressive case finding, rigorous therapy and relevant health education, were indeed followed by a reduction in the prevalence of otitis and tympanic membrane damage and an apparent general improvement in child health.

The Infectious Disease Program of the Arctic Health Research Center Public Health Service joined forces with the agencies mentioned above to provide a microbiological phase to th study. The immediate service objectives were to conduct expeditious virological and bacteriological culture of specimens taken from cases of otitis and to determine the antibiotic sensitivities of each kind of bacteria isolated from each case. The bacteriological result were forwarded as soon as possible to the field teams to allow adjustment of antibi tic therapy to the kinds of bacteria found in each case. The investigational objectives of the microbiological work were to gain information on th types of infectious agents associated with otitis media in Alaskan

native people. The objectives were also aimed at gaining some concepts of the change in the microbiology of otitis media with persistence of infection. Such information was considered to be of potential practical value to physicians faced with determining rational chemical or antibiotic therapy of otitis media in clinical situations when bacteriological diagnostic services were not available. Another aim of the microbiological study was to determine whether antibiotic therapy or prophylaxis might be in itself a determinant of the sequence of microbiological events in persistent otitis media.

CHARACTERISTICS OF POPULATION STUDIED

According to the final report of the demonstration project (3) the villages studied ranged in population from 116 to 240 with a total of 1098. Of these 546 individuals were under 17 years of age. In the group under 17 years 36.1% were Eskimo, 27.8% Indian, 20.4% of mixed racial origin, 5.9% Caucasian and 3.8% undefined. In age 6.4% of the children of the villages were under 1 year of age, 30% 1 to 4 years, 33.9% 5 to 9 years and 29.7% 10 to 14. Relatively reliable and precise information on chronology and duration of otitis was available on 130 individuals. Of these 118 were under 15 years of age. Table 1 shows their distribution by village and by age group. This table shows the seriously high prevalence of otitis among the younger age groups. The distribution by village shows great variation in prevalence of otitis. These villages were ethnically and socioeconomically dissimilar therefore these factors could account for the disparity of distribution of otitis among them.

DISTRIBUTION OF CASES BY AGE OF ONSET AND CHRONICITY

Of the 130 persons studied microbiologically the age at onset of otitis ranged from 2 to 360 months, with an arithmetic mean of 52 months. Thirty five percent of these subjects had developed suppurative otitis media with perforation of the tympanum by 1 year of age 52% (cumulatively) before 2 years of age. Thirty-eight percent of the subjects developed otitis between 2 and 10 years of age and only 10% after 10 years.

SAMPLING METHODS AND MATERIALS

The procedures and conditions of microbiological sampling were governed by the practical objectives of the study-demonstration and the field working conditions. Since the primary study objectives were casefinding and expedi

TABLE 1 *Age distribution of study population and otitis cases.*

A. *By Age Group*

Age	Total no. in age group in villages studied	Number of otitis cases studied bacteriologically	% Age group with otitis
Under 1 year	35	16	45.7
1 to 4 years	164	55	33.5
5 to 9 years	185	31	16.4
10 to 14 years	162	13	8.0

In addition, 8 of the subjects were in the 15- to 19-year-old age group, 3 in the 20- to 24-year group and 1 over age 25.

B. *Geographic*

	Aniak	Crooked Creek	Kalskag	Anvik	Holy Cross	Shageluk
No. of otitis patients	31	24	26	9	27	10
Total population	245	123	232	112	257	129
% with otitis	12.9	19.5	11.2	8.0	10.5	7.8

tious initiation of medical treatment, only the initial cultures from each case represented natural infectious flora. All subsequent or "Following" cultures were made after the subjects had been given courses of sulfonamide or antibiotic agents as well as other therapeutic treatment. The working conditions of field clinical operations did not allow sampling of acute otitis media exudate before pathologic perforation of the tympanum. Therefore none of the microbiological work reported here is equivalent to the fine investigations of Lahikainen (4) and Grönroos and associates (5) who obtained specimens of acute otitis media exudate by needle aspiration through the unruptured tympanic membrane. Likewise the itinerant character of our field operations did not allow on-site bacteriological culture of samples, but required that specimens be forwarded by air transport to the central laboratory. The methods for transmission of samples are described in a following section of this paper.

To test the relationship between pharyngeal flora and that of otitis exudate the field staff was requested to obtain a throat swab sample whenever feasible to accompany the swab specimen of ear exudate from each case. Although this was not accomplished in all cases, sufficient numbers of paired ear exudate and throat swab specimens were obtained to allow comparisons of flora from the two sites, and to study the comparative change in flora with continuation of infection.

To obtain specimens of ear exudate the field staff was instructed to clean the external auditory canal with sterile cotton swabs, without use of anti

septics, until it was free of crusted old exudate Then fresh exudate was taken with a sterilized cotton tipped applicator stick The applicator was then inserted in transmission medium for forwarding to the laboratory To obtain samples of pharyngeal flora the lateral walls, the tonsils, and the posterior wall of the pharynx were swabbed with a sterilized cotton tipped applicator The applicator tip was then plunged into transmission medium for forwarding to the laboratory

Transmission medium for bacteriological culture was a buffered agar containing heart infusion proteose-peptone, gelatin, dextrose and casein (Stock Culture Agar Difco) This was tubed, as a butt about 5 cm in depth, in screw cap glass vials or plastic friction seal vials. This medium was used in preference to a fluid or semisolid medium to prevent leakage in transit and the consequent intrusion of bacterial contamination through the closure Transmission medium for virological specimens was Earle s balanced salt solution with addition of calf serum to the concentration of 1% The medium contained sufficient amounts of penicillin streptomycin and mycostatin to prevent bacterial and fungal growth Later in the study 1% gelatin also was added to assist in viral stabilization This medium was found in other studies to be adequate as a sample transmission and maintenance medium for influenza virus, polioviruses ECHO viruses, Coxsackie viruses and adenoviruses. The virological medium was tubed in 2 ml amounts in screw cap glass vials.

The field staff was instructed to keep bacteriological samples at approximately 10 C and to keep the virological samples as cold as possible without freezing until the time of forwarding These conditions could easily be approximated in the customary village habitation by keeping the bacteriological specimens on the floor in living quarters, away from the radiant heat of stoves, and the virological specimens within insulated containers in the storm shed

These methods of sample maintenance and transmission had been tested previously by the senior author in other field operations and found to be efficacious. In those field tests, comparison of bacteriological cultures made on site in the village and cultures and made at the central laboratory one to two weeks later from simultaneously taken samples kept in transmission medium showed excellent preservation of flora in kind and quantity The virological sampling and transmission methods were also found adequate in other projects, to allow cultivation in the central laboratory of viruses as fragile as influenza which had been obtained from cases in remote sites several days previous to initiation of culture in the central laboratory These virological methods were nevertheless, inadequate for organisms such as the Respiratory Syncytial Viruses which with current sampling and cultural systems, require immediate cultivation

MICROBIOLOGICAL CULTURE METHODS

The cultural approaches and procedures were selected and devised to serve both the practical objectives of providing the field physician with early bacteriological advice and the research objectives of determining, to the greatest degree practicable, the genera and species of bacteria associated with purulent otitis media. Maximum utilization of limited laboratory facilities and personnel required a highly systematized cultural regimen. The same limitations prevented the inclusion of additional bacteriological examinations for genera or species of special interest such as anaerobic cocci, mycobacteria, or pleuropneumonia like organisms. The methods were competent to obtain pure cultures and identify about 90 species of aerobic bacteria, belonging to 23 genera, distributed among the families *Pseudomonadaceae Achromobacteraceae, Enterobacteriaceae Micrococcaceae, Neisseriaceae Lactobacillaceae* (tribe *Streptococceae*) and *Corynebacteriaceae* The scheme of morphological and biochemical tests was developed according to Bergeys Manual (6) except for the *Streptococci* which were identified according to the classification of Sherman (7) The scheme required the employment of 32 different morphological or biochemical determinations. The least number of tests required for classification within any one family was 10 (*Neisseriaceae*) the most, 19 (*Enterobacteriaceae*) In addition, hemolytic streptococci were classified antigenically by the Lancefield precipitin method.

Antibiotic sensitivity determinations were made with the use of "Bacto Unidisks" (medium concentration) The type of disks used included Penicillin (5 units) Chloromycetin (10 mcg) Tri Sulfa (150 mcg) Terramycin (10 mcg) Tetracycline (10 mcg) Erythromycin (5 mcg) Dihydrostreptomycin (5 m g) and Aureomycin (10 mcg) Late in the study when the field physician introduced Neosporin into the therapeutic array Neomycin (10 mcg) and Polymyxin (100 units) sensitivity discs were added to the array Antibiotic sensitivity tests were carried out on poured agar plates inoculated heavily with the test organisms, according to procedures recommended by the manufacturer In our tests only the medium level of concentration of each antibiotic was used, since the readings were comparative among many bacterial isolates. The laboratorians carrying out the sensitivity determination standardized their readings by frequent independent dual readings of tests and agreed on a reading of "very sensitive" for an inhibition zone greater than 0 7 cm, "moderatly sensitive for an inhibition zone of 0.25 to 0 7 cm and slightly sensitive for an inhibition zone of 0.25 cm or less. Organisms which grew to the edges of and under the antibiotic disks were considered "resistant Thi type of sensitivity determination was considered to be only roughly quantitative but adequate to assist the field physician in maki g rational selection of antibiotics for continued treatment of the individuals under study

The general bacteriological approach was as follows Each swab received for culture was streaked on a plate of stock culture agar enriched with 10% whole blood (human, type O) and incubated at 37 C for 24 to 72 hours, depending on the time required to obtain good growth of colonies. Representative colonies of each type present on each plate were picked and streaked on stock culture agar slants. If indicated by the nature of the growth serum agar or blood agar slants were used for growing stock of specific isolates. After morphological and microscopic observation to check on purity (mixed cultures were restreaked on plates for separation) antibiotic sensitivity determinations were made of each isolate and a transplant was made to provide stock for later taxonomic determinations. Thus gross morphologic classifications (gram negative rod streptococcus, micrococcus, etc.) and antibiotic sensitivity determinations on all of the isolates from a group of specimens were usually accomplished within 6 days of receipt of the specimens, and the results forwarded to the field clinical staff Taxonomic work on the isolates was carried out as time permitted

Virological specimens were cultured in tissue culture (monkey kidney and Kb cells) suckling mice and embryonated chicken eggs. The techniques used in tissue culture and suckling mouse inoculations have been described in a previous publication (8) The chick-embryo cultures employed eggs incubated for seven days previous to inoculation These were injected suballantoically with specimen fluids. The eggs were examined by transillumination daily after inoculation Moribund embryos were harvested as soon as they were detected All remaining embryos were harvested at 7 days incubation after inoculation A second passage of ground amnion and allantoic membrane from the embryos inoculated initially was made to allow additional opportunity for viral propagation At harvest both embryos and membranes were examined grossly for evidence of pathology Allantoic and amniotic fluids from each egg passage and fluids from each tissue culture passage were harvested and tested for hemagglutinating agents

GENERAL RESULTS AND ANALYSES

None of the virological specimens cultured in any of the media used yielded viral isolates. Since in other work on different disease and ecological issues, a wide variety of enteric viruses, adenoviruses and myxoviruses had been recovered by similar sampling and identical laboratory techniques, we concluded that such viruses were not present in the otitis exudate of the cases studied We could not conclude the same with respect to agents such as the Respiratory–Syncytial Viruses, which require immediate cultivation

Since a primary objective of this study was to determine the changes in flora with duration of otitis, the subject cases were classified into eight groups according to time elapsed between initial occurrence of symptoms

TABLE 2. *Isolate—Sample ratio of cultures obtained from otitis exudate*

Group	Ratio[a] Initial cultures	Ratio[a] Following cultures (Persistent cases)
I	2.6	3.3
II	3.3	4.2
III	2.5	2.6
IV	1.7	2.8
V	1.8	2.8
VI	2.4	3.6
VII	2.3	2.9
VIII	2.1	2.9
Overall	2.2	3.1

$$\text{Ratio} = \frac{\text{Total number of bacterial isolates from group}}{\text{Total number of samples in group}}$$

and the first sampling for microbiological culture. These groups, their chronological characteristics and size are as follows

Group I, duration of otitis 1 week or less, 21 individuals
Group II, duration of otitis 1 week to 1 month, 16 individuals
Group III, duration of otitis 1 month to 6 months, 19 individuals
Group IV duration of otitis 6 months to 1 year 23 individuals
Group V duration of otitis 1 year to 2 years, 14 individuals
Group VI duration of otitis 2 years to 5 years, 13 individuals
Group VII, duration of otitis 5 years to 10 years, 12 individuals
Group VIII, duration of otitis over 10 years, 11 individuals

In earlier phases of data analysis, the individuals of Group III had been divided into two groups, one with otitis duration of 1 to 2 months, and the other 2 to 6 months. However no significant difference between them was found in the kind and prevalence of bacterial species therefore, they were combined into one group for the final analysis.

Although a wide variety of bacterial species and types were encountered, no one specimen yielded a large number of isolates. Table 2 summarizes the rate of isolates per sample in the Initial and Following cultures. Each morphologically distinct colony type on each culture plate was picked for indentification, but in a large number of instances the taxonomic determinations indicated that colonial variants of the same species had been recovered These were counted as a single species isolation.

The maximum time interval between the Initial culture and last Following culture serves as a measure of persistence or recurrence of exudative otitis in the cases under study The case-distribution by maximum interval is given for each group in Table 3.

In 6% of the cases, otitis did not persist beyond four months after

TABLE 2. *Isolate—Sample ratio of cultures obtained from otitis exudate.*

Group	Ratio[a] Initial cultures	Ratio[a] Following cultures (Persistent cases)
I	2.5	3.3
II	3.3	4.2
III	2.5	2.6
IV	1.7	2.8
V	1.8	2.9
VI	2.4	3.6
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The maximum time interval between the Initial culture and last Following culture serves as a measure of persistence or recurrence of exudative otitis in the cases under study The case-distribution by maximum interval is given for each group in Table 3

In 8% of the cases, otitis did not persist beyond four months after

The general bacteriological approach was as follows Each swab received for culture was streaked on a plate of stock culture agar enriched with 10% whole blood (human type O) and incubated at 37 C for 24 to 72 hours, depending on the time required to obtain good growth of colonies. Representative colonies of each type present on each plate were picked and streaked on stock culture agar slants. If indicated by the nature of the growth serum agar or blood agar slants were used for growing stock of specific isolates After morphological and microscopic observation to check on purity (mixed cultures were restreaked on plates for separation) antibiotic sensitivity determinations were made of each isolate and a transplant was made to provide stock for later taxonomic determinations. Thus gross morphologic classifications (gram-negative rod, streptococcus, micrococcus, etc.) and antibiotic sensitivity determinations on all of the isolates from a group of specimens were usually accomplished within 6 days of receipt of the specimens, and the results forwarded to the field clinical staff Taxonomic work on the isolates was carried out as time permitted

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II	2.3	4.2
III	2.6	2.6
IV	1.7	2.8
V	1.6	2.0
VI	2.4	3.0
VII	2.3	2.9
VIII	2.1	2.9
Overall	2.3	3.1

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Group VI duration of otitis 2 years to 5 years, 13 individuals
Group VII, duration of otitis 5 years to 10 years, 13 individuals
Group VIII, duration of otitis over 10 years, 11 individuals

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Although a wide variety of bacterial species and types were encountered, no one specimen yielded a large number of isolates. Table 2 summarizes the rate of isolates per sample in the *Initial* and Following cultures. Each morphologically distinct colony type on each culture plate was picked for indentification, but in a large number of instances the taxonomic determinations indicated that colonial variants of the same species had been recovered. These were counted as a single species isolation.

The maximum time interval between the Initial culture and last Following culture serves as a measure of persistence or recurrence of exudative otitis in the cases under study The case-distribution by maximum interval is given for each group in Table 3.

In 76% of the cases, otitis did not persist beyond four months after

TABLE 3 *Percentage distribution of cases by interval between first and last culture*

Group	I	II	III	IV	V	VI	VII	VIII	Average Overall
One culture only	42.8	50 0	30.8	47 7	21.3	23.1	61 0	27.3	10 0
2 Months interval	9 5	12.5	10.5	4.3	14 2	7 7		18.2	9.2
3 Months interval	14 2	25.0	4.3	8.7		23.1		18.2	11 6
4 Months interval	19 0		15.8	13.0	28.4	23.7	7 7	18.2	15 1
5 Months interval				4.3					0.8
6 Months interval	4 8								0.8
7 Months interval			5.3	4.3				9 1	2.3
8 Months interval		6.3							0.8
10 Months interval	4 8			8.7	7 1		15.4		4 6
12 Months interval	4 8	6.3					7 7		2.3
14 Months interval						7 7		9 1	1.5
16 Months interval			5.3		7 1	7 7			2.3
18 Months interval			15.8		21.3				4 6
21 Months interval			5.3	8 7		7 7	7 7		3 9

treatment was initiated Groups I II and VIII showed the lower rates of persistence of infection beyond four months, while Groups III V and VII had the higher No infections in Groups I and II were found beyond 12 months after initial culture, while in Groups III IV VI and VII cases with purulent exudate were found 18 to 21 months after initial diagnosis. The data indicate that infections which have been established a month or more before treatment is begun are more likely to be resistant to therapy than those infections which are treated at an earlier stage This is not a new thought The data merely underscore the accepted desirability of early diagnosis and treatment Nevertheless it is encouraging to note that even with cases that had been chronic or recurrent over a number of years, treatment to the extent allowed by itinerant nursing and medical services led to remission of the large majority of cases within a few months.

It is of pathogenetic significance to know the anatomic extent of involvement Accordingly we determined whether the involvement was unilateral or bilateral at the time of initial sampling The same was tabulated for the Following cultures on cases which were recurrent or chronic. Table 4 summarizes the findings.

Table 4 presents some interesting variations, from group to group with regard to the anatomic involvement But no distinct pattern is discernible except that at least a third of the patients with persistent purulent perforating otitis had bilateral involvement within a few months, including some of those treated within one week of onset of symptoms. The cases with eventual bilateral involvement comprised a large majority of the persistent or recurrent cases This is deduced from comparisons of the data of Tables 3 and 4

TABLE 4 *Ear involved in otitis (% of cases)*

Group	I	II	III	IV	V	VI	VII	VIII	Overall
Ear involved at time of first culture									
Right only	61.9	25.0	47.2	30.4	28.4	7.7	38.5	45.5	37.0
Left only	19.0	56.3	15.8	39.1	42.6	30.8	46.2	45.5	35.4
Both	4.8	12.5	21.0	8.7	14.3	23.1	15.4		12.3
Untreated	14.3	6.3	15.8	21.7	14.2	38.5		9.1	15.4
Ear involved, including Following cultures									
Right only	47.6	18.8	36.8	26.0	21.3	15.4	38.5	45.5	31.6
Left only	14.3	43.8	15.8	34.7	28.4	30.8	38.5	27.3	28.5
Both	33.3	37.5	42.1	26.0	42.6	46.2	23.1	27.3	21.7
Untreated	4.8		5.3	13.0	7.1	7.7			5.4

RESULTS—BACTERIOLOGICAL

The taxonomic identification of several thousand isolates of "wild" bacterial strains is an exercise in judgement and interpretation rather than that of mechanical adherence to precise criteria. In many instances the taxonomic determination made upon the basis of the morphological and biochemical characteristics of an isolate was that of "most probable species" Occasionally an isolate could be assigned to a genus, but would not fit most of the criteria for any one species In such a case the species was left undetermined. With certain genera such as *Achromobacter* or *Flavobacterium*, which were generally of very low prevalence, no attempt was made to determine the species of the isolate Our experience with taxonomic identification of wild strains is not unique Indeed, taxonomic problems are to be expected in large scale isolation and identification of saprophytes which are facultatively and incidentally pathogenic.

Various modes of statistical representation of the microbial flora in otitis were tried. We found that analysis by case-prevalence was the more relevant to our epidemiologic and ecologic objectives. It was considered to be more important that we should determine the probability of occurrence of a species in a given class of cases of otitis than to determine the relative importance of a species in relation to all other bacterial species encountered in otitis. Furthermore in comparison of prevalences among species, case prevalence was considered to be a more absolute measure of their pathoecologic importance

Except for the *Streptococci* (particularly in pharyngeal cultures) and the *Staphylococci*, it was rare to find more than one species of a genus in a single culture of an ear or throat specimen. Consequently the case-prevalence of a genus could be determined with considerable validity by summarization of the case prevalences of the constituent species. This has been

TABLE 5 *Case prevalence in percent of various bacterial taxonomic groups in initial cultures of otitis exudate in relation to chronicity*

	Groups								
	I	II	III	IV	V	VI	VII	VIII	Overall
Pseudomonas (species undetermined)	5							9	1.5
Pseudomonas aeruginosa	5	6	5	9				9	4.6
Pseudomonas pseudomallei		6	5					9	3.1
Pseudomonas caviae	5	6	5						2.3
Pseudomonas fluorescens	5	13	5		7	8	8		5.4
Total for *Pseudomonadaceae* (family)	20	31	20	9	7	8	8	27	16.9
Alcaligenes (species undetermined)							8	18	2.3
Alcaligenes fecalis	14		10			8	8		5.4
Alcaligenes metalcaligenes	5	13	10		7			9	5.4
Alcaligenes bookeri		6		9					2.3
Achromobacter (species undetermined)					7	8		9	2.3
Flavobacterium (species undetermined)					7	8	8		2.3
Total for *Achromobacteriaceae* (family)	19	19	20	9	21	24	4	36	20.0
Escherichia freundii	5		5	4		8			3.1
Aerobacter aerogenes			10			15			3.1
Aerobacter cloacae	5				7				1.5
Klebsiella (species undetermined)	5	6						9	2.3
Klebsiella pneumoniae						8			0.7
Klebsiella ozenae	5			9	14				3.9
Paracolobactrum intermedius				4					0.7
Total for *Escherichiae* (tribe)	20	6	15	17	21	31		9	15.3
Proteus (species undetermined)	5	6		4					2.3
Proteus vulgaris				4					0.7
Proteus mirabilis		13	5	26	7	23	8	9	11.5
Proteus morgagni			10	4	14			9	4.6
Proteus rettgeri		6	5	4	7				3.1
Proteus inconstans			15		7	8		18	5.4
Total for genus *Proteus*	5	[illegible]	35	42	35	31	8	36	27.6
Micrococcus (species undetermined)	5			9		15	15		5.4
Micrococcus ureae	5				7				1.5
Micrococcus freundreichii		6	5						1.5
Micrococcus flavus	5								0.7
Micrococcus candidus	5	6		9	7	8			4.6
Micrococcus conglomeratus						8			0
Micrococcus varians	14	6	5	9	7		8	9	7.7
Total for genus *Micrococcus*	31	18	10	27	21	31	23	9	22.1
Staphylococcus aureus	48	81	36	9	7		39	27	31.6
Staphylococcus epidermidis	14	19	20	4		15	39	9	14.6
Total for genus *Staphylococcus*	62	100	56	13	7	15	78	36	46.2
Gaffkya tetragena			5	4					1.5
Sarcina (species undetermined)						8			0.7
Diplococcus pneumoniae	6								0.7
Neisseria (species undetermined)		6					8		1.5
Neisseria catarrhalis		19				8		18	3.9
Total, genus *Neisseria*		25				8	8	18	5.1

Table 5 (*continued*)

	Groups								
	I	II	III	IV	V	VI	VII	VIII	Overall
Streptococcus, Group A	5								0.7
Streptococcus, Group C	5	13	5			8			2.1
Streptococcus pyogenes (untyped)				4	7				1.5
Streptococcus salivaris	23	19	26	9	14	23	31	18	18.5
Streptococcus mitis				9	7			9	2.1
Streptococcus, equinus		6							0.7
Streptococcus fecalis	14	38	15	9			15		12.3
Streptococcus lactis			5						0.7
Total for *Streptococcus*	57	76	51	31	28	31	46	27	40.6
Corynebacterium (species undetermined)			15	4			8		2.9
Corynebacterium enzymicum	10	13	5	4		15	15		6.2
Corynebacterium striatum	10		5			15	8		3.1
Corynebacterium pseudotuberculosis	5								0.7
Corynebacterium xerosis	10	6			7	8			3.1
Corynebacterium pseudodiphthericum		6	5	9	7	8	15	9	6.2
Corynebacterium parvum	5								0.7
Total for genus *Corynebacterium*	40	25	30	17	14	46	46	9	23.9
Hemophilus (species undetermined)						8			0.7

See p. 11 for definition of Groups.

done to eliminate excessive detail in a number of comparative tabulations in this paper

Table 5 change presents the case-prevalence of genera and species of bacterial flora cultivated from the initial exudate specimens taken from the 130 subjects of this study The information is summarized in Figure 1 The data are tabulated in reference to the eight Groups or classes of cases previously described (p. 11) It is evident that the flora found in purulent otitis media is highly variable and involves a large number of species and types—41 in this case not including a few genera within which species identification was not attempted. Very few species occur in a significantly large proportion of cases. The exceptions are the following *Proteus mirabilis* had a case prevalence over 20% in two Groups. *Staphylococcus aureus* was found in highly significant prevalence in five Groups, ranging from 27% to 81% *Staphylococcus epidermidis* also occurred in significant proportion in five Groups, ranging from 14% to 39% *Neisseria catarrhalis* w prevalent in significant proportions in two Groups. Of the streptococci, only *S salivarius* and *S faecalis* appeared to be significant in otitis flora, but not even these species attained great prevalence in any of the patient Groups. It is clear that in this series of otitis cases no ne species of bacteria can be a signed, verall, a predominant etiological role

There are interesting shifts in prevalence of species and genera, from Group to Group, indicating ecological change in relation to duration of in

Table 5 *Case prevalence in percent of various bacterial taxonomic groups in initial cultures of otitis exudate in relation to chronicity*

	Groups								
	I	II	III	IV	V	VI	VII	VIII	Overall
Pseudomonas (species undetermined)	5							9	1.5
Pseudomonas aeruginosa	5	6	5	9				9	4.6
Pseudomonas pseudomallei		6	5					9	3.1
Pseudomonas caviae	5	6	5						2.3
Pseudomonas fluorescens	5	13	5		7	8	8		5.4
Total for *Pseudomonadaceae* (family)	20	31	20	9	7	8	8	27	16.9
Alcaligenes (species undetermined)							8	18	2.3
Alcaligenes fecalis	14		10			8	8		5.4
Alcaligenes metalcaligenes	5	13	10		7			9	5.1
Alcaligenes bookeri		6		9					2.3
Achromobacter (species undetermined)					7	8		0	2.3
Flavobacterium (species undetermined)					7	8	8		2.3
Total for *Achromobacteriaceae* (family)	19	19	20	9	21	24	24	36	20.0
Escherichia freundii	5		5	4		8			3.1
Aerobacter aerogenes			10			15			3.1
Aerobacter cloacae	5				7				1.5
Klebsiella (species undetermined)	5	6						9	2.3
Klebsiella pneumoniae						8			0.7
Klebsiella ozenae	5			9	14				3.9
Paracolobactrum intermedius				4					0.7
Total for *Escherichiae* (tribe)	20	6	15	17	21	31		9	15.3
Proteus (species undetermined)	5	6		4					2.3
Proteus vulgaris				4					0.7
Proteus mirabilis		13	5	26	7	23	8	9	11.5
Proteus morgagni			10	4	14			0	4.6
Proteus rettgeri		6	5	4	7				3.1
Proteus inconstans			15		7	8		18	5.4
Total for genus *Proteus*	5	25	35	42	35	31	8	30	27.6
Micrococcus (species undetermined)	5			9		15	15		5.1
Micrococcus ureae	5				7				1.5
Micrococcus freundreichii		6	5						1.5
Micrococcus flavus	5								0.7
Micrococcus candidus	5	0		9	7	8			4.6
Micrococcus conglomeratus						8			0.7
Micrococcus varians	14	6	5	0	7		8	0	7.7
Total for genus *Micrococcus*	31	18	10	27	21	31	23	9	22.1
Staphylococcus aureus	48	81	36	9	7		39	27	31.6
Staphylococcus epidermidis	14	19	20	4		15	39	9	11.6
Total for genus *Staphylococcus*	62	100	56	13	7	15	78	36	48.2
Gaffkya tetragena			5	4					1.5
Sarcina (species undetermined)						8			0.7
Diplococcus pneumoniae	0								0.7
Neisseria (species undetermined)		6					8		1.5
Neisseria catarrhalis		19				8		18	3.9
Total, genus *Neisseria*		25				8	8	18	5.1

TABLE 6 *Case prevalence in percent of various bacterial taxonomic groups in initial pharyngeal cultures from otitis patients, by chronicity of otitis*

	Groups								
	I	II	III	IV	V	VI	VII	VIII	Overall
Pseudomonas aeruginosa	14			25					4.9
Pseudomonas [illegible]		18	10						3.5
Pseudomonas fluorescens	7	18	40					20	10.8
Total for genus *Pseudomonas*	21	38	50	25				20	19.2
Alcaligenes (species undetermined)						20			2.5
Alcaligenes fecalis	7		10				20		4.6
Alcaligenes metalcaligenes						20			2.5
Achromobacter (species undetermined)		9		13					2.5
Flavobacterium (species undetermined)									
Total for *Achromobacteriaceae*	7	9	10	13		40	20		12.1
Escherichia coli		9	10						2.5
Escherichia freundii	7	27	10						5.5
Aerobacter aerogenes		9		25					4.3
Aerobacter cloacae	14								1
Klebsiella (species undetermined)	7						20		3.4
Klebsiella ozaenae					25				2.1
Klebsiella rhinoscleromatis				13					1.4
Paracolobactrum (species undetermined)				13					1.4
Paracolobactrum intermedium			10				20		2.7
Paracolobactrum arizonae	7								0.9
Total for tribe *Escherichiae*	35	45	30	50	25		40		27.9
Proteus (species undetermined)				13		20			3.3
Proteus vulgaris	7		10						3.3
Proteus mirabilis	7	9	10						4.9
Proteus morgagni			10	13				20	4.9
Proteus inconstans				13		20			3.3
Total for genus *Proteus*	14	9	30	38		40		20	19.7
Micrococcus (species undetermined)	7	9		13			20		6.1
Micrococcus luteus								20	2.5
Micrococcus freudenreichii		9			25		20		6.7
Micrococcus candidus	7	9						20	4.5
Micrococcus varians	7	9		25			40	20	12.6
Total for genus *Micrococcus*	21	36		38	25		60	80	32.4
Staphylococcus aureus	14	27	20	25	25		40	20	21.4
Staphylococcus epidermidis	7	18		38					7.9
Total for genus *Staphylococcus*	21	45	20	63	23		40	20	29.3
Neisseria catarrhalis			20						2.5
Neisseria sicca			10						1.2
Total for genus *Neisseria*			20						3.7
Streptococcus, Group A	14	18	10	13			20		9.4
Streptococcus, Group C	14	9							2.9
Streptococcus, Group G		9							1.1
Streptococcus pyogenes (untyped)			20		25			20	6.1
Streptococcus salivarius	27	37	30	38	23	40	20	40	30.8



Fig. 1. Comparison of flora of ear and pharyngeal cultures in otitis.

fection. This is more evident when case prevalences are summarized within bacterial genera or families. The resultant pattern is evident in Figure 1. The bacterial groups compared in this figure are not taxonomically equivalent. Six are genera (*Pseudomonas, Proteus, Micrococcus, Staphylococcus, Streptococcus* and *Cornyebacterium*). One is a family (*Achromobacteraceae*) represented by genera *Achromobacter, Flavobacterium* and *Alcaligenes* in our isolates. One is a tribe (*Escherichieae*) represented by genera *Escherichia, Aerobacter, Klebsiella* and *Paracolobactrum*. To test the validity of using cumulative case prevalences in this comparison, the sum of prevalences of species in each genus or family was compared with the expected number of isolates calculated from the average number of isolations per case (see "Ratio" column for initial cultures, Table 2). The differences between the actual and calculated prevalences were comparatively small. In those instances where the actual cumulative prevalence exceeded the calculated, more than one species of a genus had occurred in a few samples. Where the cumulative prevalence was less than the calculated, a few minor species had not been included in the comparison.

Bearing in mind the duration of otitis in each patient Group (see p. 11) and the detailed case prevalences of species (Table 5), the comparisons of initial cultures illustrated by Figure 1 are patho-ecologically significant. In the cases with duration of 6 months or less (Groups I, II and III) the preponderant flora, by far, were the gram positive cocci (*Staphylococcus* and

TABLE 7 *Comparative distribution of various bacterial genera and species in ear exudate and in throat samples of otitis patients.*

	Ear	Throat		Ear	Throat		Ear	Throat
Pseudomonas			*Proteus*			*Streptococcus*		
aeruginosa			*vulgaris*			Group A		
pseudomallei		–	*mirabilis*			Group C		
caviae			*morganii*			Group G	–	
fluorescens			*rettgeri*		–	*Streptococcus* (cont'd)		
Alcaligenes			*inconstans*			*pyogenes* (untyped)		
faecalis			*Micrococcus*			*salivarius*		
metalcaligenes			*luteus*	–		*mitis*		
bookeri		–	*ureae*		–	*equinus*		
Achromobacter			*freudenreichii*			*faecalis*		
Flavobacterium		–	*flavus*		–	*lactis*		–
Escherichia			*candidus*			*Corynebacterium*		
coli	–		*conglomeratus*		–	*enzymicum*		
freundii			*varians*			*hoagii*	–	
Aerobacter			*Staphylococcus*			*striatum*		–
aerogenes			*aureus*			*pseudotuberculosis*		–
cloacae			*epidermidis*			*xerosis*		–
Klebsiella			*Gaffkya*		–	*pseudodiphtheriticum*		
pneumoniae		–	*Sarcina*		–	*acnes*		–
ozaenae			*Neisseria*			*parvum*		
rhinoscleromatis		–	*catarrhalis*			*Haemophilus*		–
Paracolobactrum			*sicca*	–				
intermedium								
arizonae		–						

– Present. ~ = Not present

were not found in otitis exudate cultures. The distribution of genera and species in the throat and otitis exudate cultures is summarized in Table 7 There was no one species of greater prevalence in the otitis flora of this a semblv f cases which was not also found in the throat flora.

Although in most instances the same genus or family of bacteria was found in both ear exudate and in the throats of persons having otitis, the prevalence in one site was rarely equivalent to the other Indeed there was often con iderable disparity This can be viewed as being etiologically significant in some comparisons for instance in Figure 1 note the much greater prevalence of *St phylococci* in ear exudate than in throat cultures in Groups I II III, VII and VIII as well as the inversion of this disparity in Groups IV and V In contradistinction, the *Streptococci* were almost con si tently les prevalent in ear exudate than they were in throat flora of these patient Groups. These *trends* in comparative prevalence might be taken to indicate a more pathogenetically significant role and invasive activ ity for st phlococci in acute early chronic and late recurrent otitis than

Table 6 (*continued*)

	Groups								
	I	II	III	IV	V	VI	VII	VIII	Overall
Streptococcus mitis	7								0 9
Streptococcus equinus		18							2.2
Streptococcus fecali	7	9		13					3.6
Total for genus *Streptococcus*	69	90	60	61	50	40	40	60	59 1
Corynebacterium (species undetermined)			10						1 1
Corynebacterium enzymicum	7							20	3.3
Corynebacterium hoagii	14						40	20	9.2
Corynebacterium pseudodiphthericum	7							20	3.3
Corynebacterium acnes	7						20		3.3
Corynebacterium parvum				13					1 1
Total for genus *Corynebacterium*	35		10	13			60	60	21.8

See p 11 for definition of Groups.

Streptococcus) In the cases with duration lying between 6 months and 5 years (Groups IV V and VI) the prevalence of the cocci was greatly reduced and the prevalence of gram negative organisms was greatly increased especially *Proteus* In cases of extreme duration—between 5 and over 10 years (Groups VII and VIII)—there was a resurgence of *Streptococci* and *Staphylococci* while the gram negatives showed a loss of prevalence in Group VII but considerable resurgence in Group VIII *Pseudomonas* prevalences did not follow the trends of other gram negative bacteria but mimicked the trends of *Staphylococci* and *Streptococci* The variance in *Cornyebacterial* prevalences by patient groups followed those of *Staphylococcus* and *Streptococcus* except for an earlier resurgence No distinct pattern is apparent in the graph of *Micrococcus* prevalences. It is also interesting to note a considerably lower ratio of isolations per case in the mid range (Groups IV and V) indicating a trend towards predominance of one bacterial species in the exudate of infection in cases with duration of six months to two years The general predominance of gram positive organisms in Groups VII and VIII may indicate that these were for the most part, cases of reinfection rather than of persistent otitis

In 61 out of 130 cases, at the time of initial sampling of otitis exudate and prior to treatment a pharyngeal swab specimen was also taken in order to compare throat and otitis flora The bacteriological findings from the throat cultures are presented in detail in Table 6 and compared graphically in Figure 1 Comparison shows that most of the genera and species found in otitis flora were also found in throat flora Out of 17 genera found in exudate flora only four of minor importance (*Flavobacterium Gaffkya Sarcina* and *Haemophilus*) were not found in the throat samples Out of a total of 41 species found in the otitis exudate cultures, 30 were also found in the throat cultures Only 8 out of 38 species found in the throat cultures

Escherichia Paracolons and *Proteus* are not common normal throat flora of the people studied, (2) that their presence in otitis may be due to external contamination and (3) that their presence in the pharynx of otitis patients may be a retrograde contamination of the pharynx via the Eustachian tube. The latter hypothesis is ecologically intriguing, but would require more bacteriological proof for its substantiation.

To explore the possibility of geographic ecological effects, the prevalence of the various genera and species of bacteria were tabulated with regard to the village of origin of the cases. This was done with the data of both the otitis exudate and pharyngeal swab specimens. At first there appeared to be some ecological variation in distribution of kinds of bacteria from village to village. For instance the case prevalences of *Staphylococci* in exudate cultures were respectively 58.5%, 20.7%, 29.6%, 52.6%, 48.5% and 0 in villages 1 through 6. The prevalences of *Proteus* in the same series were respectively 13.0%, 24.1%, 33.3%, 27.9% and 57.1%. To check the validity of these observations the distribution of cases, by chronicity was also tabulated by village. When the case-chronicity distribution was checked against the bacterial genera and species distribution, the geographic *factor* was eliminated from consideration. In other words, the distribution of genera and species of bacteria in otitis among the villages followed the distribution of cases by chronicity. For example, in villages where cases classified in Groups III, IV and V predominated, the prevalence of *Staphylococci* was low and of *Proteus* relatively high. In villages where cases of Groups I, II, III, VII, and VIII predominated, the prevalence of *Staphylococci* was high and of *Proteus* relatively low (consult Figure 1 to see the basis of correlation).

Thus, geographic ecological factors did not appear to be significant in this study. This observation cannot be extrapolated to apply to *comparisons* between more widely separated geographic areas. The author has, in other studies, gained evidence of significant involvement of geographic discontinuity in the distribution of viral agents and diseases (8, 9 *and 10*) and of pharyngeal flora (11) among residents of various areas in the American Arctic. Similarly the comparison of otitis flora from areas more widely separated than those reported here may reveal geographic ecological factors.

In the course of successive visits to the study villages, each time the project nurses or physicians examined a person with persistent or recurrent otitis, a swab sample was taken for microbiological evaluations. The overall isolate ratios of these "Following" cultures are shown in Table 2 and the distributions of intervals between first and last cultures are shown in Table 3. The case-prevalences of various species and cumulative case-prevalences of various species and cumulative case-prevalences of species within genera, according to duration of otitis, are summarized in Table 9 and compared in Figure 2. In interpretation of the ecological significance of these data, it must be remembered that all of the "*Following*" cultures were derived from patients under treatment with antibiotics and sulfonamides. The bac

TABLE 8 *Comparison of genera represented and numbers of species within genera found in throat cultures from otitis patients and from normal school children*

	Number of Species	
	Patients	Normals
Pseudomonas	3	3
Alcaligenes	3	2
Achromobacter	×	×
Flavobacterium	0	×
Escherichea	2	0
Aerobacter	2	1
Klebsiella	1	1
Paracolobactrum	2	0
Proteus	4	0
Micrococcus	4	1
Staphylococcus	2	2
Neisseria	2	2
Streptococcus	8	9
Corynebacterium	5	2
	38	23

× = genus represented species not determined.

is characteristic of streptococci No general patterns are discernible in the ear–throat flora relationships of the other genera and species however if the number of samples had been larger a significant pattern might have emerged for these species of low prevalence The overall comparisons (last column) might be interpreted to indicate that the bacterial groups of greater etiological significance, by virtue of greater prevalence in ear exudate over that found in the throat were the genera *Staphylococcus Proteus Corynebacterium* and family *Achromobacteriaceae* (primarily genus *Alcaligenes*) Undoubtedly the *Streptococcus* group was also highly significant from the etiological standpoint but its prevalence *in the throat* consistently outstripped its prevalence in otitis exudate

To check on the normalcy of the throat flora of otitis patients, throat swab samples were taken from 54 children and youths attending a boarding school in a village in the same general geographic area as the demonstration villages. None of these children had otitis at the time of the sampling The representation of bacterial genera and species in these samples in comparison with the throat flora of patients is summarized in Table 8 For the most part the *same genera* were represented the more notable exceptions being the absence of *Escherichia Paracolobactrum* and *Proteus* species in the samples from the normal individuals In addition the normal throat flora contained fewer species representing those genera which were found in both the otitis cases and the control subjects. These results suggest (1) that

Escherichia Paracolons and *Proteus* are not common normal throat flora of the people studied, (2) that their presence in otitis may be due to external contamination and (3) that their presence in the pharynx of otitis patients may be a retrograde contamination of the pharynx via the Eustachian tube. The latter hypothesis is ecologically intriguing, but would require more bacteriological proof for its substantiation.

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Thus, geographic ecological factors did not appear to be significant in *this study* This observation cannot be extrapolated to apply to comparisons between more widely separated geographic areas. The author has, in other studies, gained evidence of significant involvement of geographic discontinuity in the *distribution* of viral agents and diseases (8, 9, and 10) and of pharyngeal flora (11) among residents *of* various areas in the American Arctic. Similarly the comparison of otitis flora from areas more widely separated than those reported here may reveal geographic ecological factors.

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	Patients	Normals
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Alcaligenes	3	2
Achromobacter	×	×
Flavobacterium	0	×
Escherichea	2	0
Aerobacter	2	1
Klebsiella	1	1
Paracolobactrum	2	0
Proteus	4	0
Micrococcus	4	1
Staphylococcus	2	2
Neisseria	2	2
Streptococcus	8	9
Corynebacterium	5	2
	38	23

× = genus represented, species not determined.

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Table 9 (*continued*)

	Initial cultures	Following cultures (months after)			
		2	3–5	6–8	Over 8
Neisseria (species undetermined)	1.5	4	2	0	3
Neisseria catarrhalis	4.6	4	14	4	3
Neisseria sicca	0	0	4	0	3
Total for genus *Neisseria*	6.1	8	20	4	9
Streptococcus, Group A	0.8	4	5	0	8
Streptococcus Group C	3.9	7	9	4	14
Streptococcus, Group E	0	0	2	0	11
Streptococcus pyogenes (untyped)	1.5	0	0	0	3
Streptococcus salivarius	21.6	22	9	0	3
Streptococcus mitis	3.1	4	9	4	3
Streptococcus equinus	0	0	0	0	0
Streptococcus anginosus	0	4	0	0	3
Streptococcus zymogenes	0	0	2	4	0
Streptococcus faecalis	12.3	7	32	12	59
Streptococcus lactis	0.8	0	0	0	0
Total for genus *Streptococcus*	44 0	47	75	24	101
Corynebacterium (species undetermined)	3.9	4	7	12	36
Corynebacterium enzymicum	6.2	7	0	0	0
Corynebacterium hoagii	1.5	4	2	0	0
Corynebacterium striatum	4.6	4	0	0	0
Corynebacterium pseudotuberculosis	0.8	0	2	0	0
Corynebacterium xerosis	3.9	0	4	0	0
Corynebacterium pseudodiphthericum	6.9	0	0	0	0
Corynebacterium acnes	0	0	2	0	14
Corynebacterium parvum	0 8	4	0	0	0
Corynebacterium pyogenes	0	0	4	0	0
Total for genus *Corynebacterium*	28.6	21	20	12	50
Hemophilus (species undetermined)	0.8	0	8	0	0
Number of Cases	130	28	66	25	36

teria found in the Following cultures were those that persisted in spite of therapy therefore, they were not the natural flora of untreated, persistent otitis media. The otitis persistence categories, in this analysis, fell naturally into 2 months, 3 to 5 months, 6 to 8 months, and over 8 months. For comparison with the Following cultures, the overall tabulations for the Initial cultures are also given in Table 9 and graphed in Figure 2.

There are som striking differences in species and genera distribution of the cultures from treated cases as compared with untreated cases. Note that both *Pseudomonas* and *Alcaligenes* species reached levels of case-prevalence considerably greater than that found in the "natural" otitis flora (Initial cultures) This is also true of prevalences of *Proteus* species in those cases which persisted over 8 months. Except for the 6 to 8 month group, *Strepto-*

TABLE 9 *Case prevalence (percent) of various bacterial taxonomic groups in cultures of otitis exudate Comparison of Initial cultures and Following cultures at 2 3 to 5 6 to 8 and over 8 months*

	Initial cultures	Following cultures (month after)			
		2	3–5	6–8	Over 8
Pseudomonas (species undetermined)	1.5	7	0	4	3
Pseudomonas aeruginosa	4 6	0	7	4	17
Pseudomonas pseudomallei	2.3	0	2	4	6
Pseudomonas caviae	2,3	0	7	0	14
Pseudomonas fluorescens	5,4	0	14	20	11
Total for genus *Pseudomonas*	16,1	7	30	32	51
Alcaligenes (species undetermined)	2.3	14	0	0	11
Alcaligenes fecalis	6.2	0	13	8	22
Alcaligenes metalcaligenes	4 6	0	13	8	6
Alcaligenes bookeri	2.3	0	4	0	0
Achromobacter (species undetermined)	2.3	0	7	0	0
Flavobacterium (species undetermined)	2.3	4	0	0	0
Total for family *Achromobacteriaceae*	20.0	18	37	16	42
Escherichea freundii	3.1	0	9	8	8
Aerobacter aerogenes	3 1	0	2	4	13
Aerobacter cloacae	1 5	0	2	0	0
Klebsiella (type undetermined)	1.5	0	2	0	0
Klebsiella pneumoniae	0.8	4	0	0	0
Klebsiella ozenae	3.9	0	0	8	0
Paracolobactrum intermedius	0.8	4	5	0	3
Total for tribe *Escherichea*	14 7	8	20	20	1
Proteus (species undetermined)	2.3	4	4	0	3
Proteus vulgaris	0 8	0	4	0	8
Proteus mirabilis	11 6	11		0	30
Proteus morgagni	4 6	7	11	32	26
Proteus rettgeri	3.1	0	4	0	0
Proteus inconstans	5 4	7	1	0	8
Total for genus *Proteus*	27 8	29	27	32	75
Micrococcus (species undetermined)	5.4	14	13	8	11
Micrococcus ureae	1 5	7	0	0	0
Micrococcus freundreichii	1.5	11	4	0	0
Micrococcus flavus	0.8	0	0	0	0
Micrococcus candidus	4 0	22	0	0	0
Micrococcus conglomeratus	0.8	0	0	0	0
Micrococcus varians	7 7	18	5	4	0
Total fo genus *Micrococcu*	22.3	72	22	12	11
Staphylococcus aureus	31 6	22	31	1	18
Staphylococcus epidermidis	11 6	7	27	28	11
Total for genus *Staphylococcus*	40 2	20	58	32	59
Gaffkya tetragena	1 5	4	0	4	3
Sarcina (species undetermined)	0.8	0	0	0	0
Diplococcus pneumoniae	0	0	0	4	3

Table 9 (*continued*)

	Initial cultures	Following cultures (months after)			
		2	3–5	6–8	Over 8
Neisseria (species undetermined)	1.5	4	2	0	3
Neisseria catarrhalis	4.6	4	14	4	3
Neisseria sicca	0	0	4	0	3
Total for genus *Neisseria*	6.1	8	20	4	9
Streptococcus, Group A	0.8	4	5	0	8
Streptococcus, Group C	3.5	7	9	4	14
Streptococcus, Group E	0	0	2	0	11
Streptococcus pyogenes (untyped)	1.5	0	0	0	3
Streptococcus salivarius	21.6	22	9	0	3
Streptococcus mitis	3.1	4	9	4	3
Streptococcus equinus	0	0	0	0	0
Streptococcus sanguis	0	4	0	0	3
Streptococcus zymogenes	0	0	2	4	0
Streptococcus faecalis	12.3	7	32	12	59
Streptococcus lactis	0.8	0	0	0	0
Total for genus *Streptococcus*	44.0	47	75	24	104
Corynebacterium (species undetermined)	3.9	4	7	12	36
Corynebacterium enzymicum	6.2	7	0	0	0
Corynebacterium hoagii	1.5	4	2	0	0
Corynebacterium striatum	4.6	4	0	0	0
Corynebacterium pseudotuberculosis	0.8	0	2	0	0
Corynebacterium xerosis	3.9	0	4	0	0
Corynebacterium pseudodiphthericum	6.9	0	0	0	0
Corynebacterium acnes	0	0	2	0	14
Corynebacterium parvum	0.8	4	0	0	0
Corynebacterium equi	0	0	4	0	0
Total for genus *Corynebacterium*	28.6	21	20	12	50
Haemophilus (species undetermined)	0.8	0	0	0	0
Number of Cases	130	28	56	25	38

teria found in the Following cultures were those that persisted in spite of therapy therefore, they were not the natural flora of untreated, persistent otitis media. The otitis persistence categories, in this analysis, fell naturally into 2 months, 3 to 5 months, 6 to 8 months, and over 8 months. For comparison with the Following cultures, the overall tabulations for the Initial cultures are also given in Table 9 and graphed in Figure 2.

There are some striking differences in species and genera distribution of the cultures from treated cases as compared with untreated cases. Note that both *Pseudomonas* and *Alcaligenes* species reached levels of case-prevalence considerably greater than that found in the "natural" otitis flora (Initial cultures) This is also true of prevalences of *Proteus* species in those cases which persisted over 8 months. Except for the 6 to 8 month group, *Strepto-*

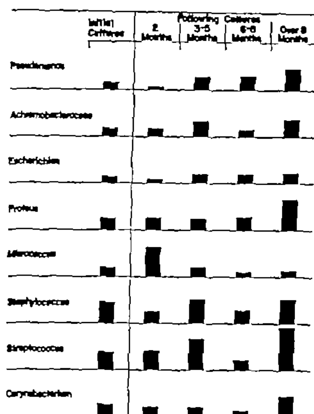


Fig 2 Comparison of flora component of initial and following cultures.

cocci showed a large increase in prevalence in the otitis cases of longer duration a considerable proportion of this increase was due to *Enterococci* The case-prevalence of *Corynebacteria* also reached a significantly high level in the cases of greatest duration *Stapyhlococcus* prevalence fluctuated but this did not reach significantly greater peak levels than those found in *untreated cases From Table 2 it can be noted that there was a general trend* towards a larger number of isolations per sample in the Following cultures. This is corroborated in detail by the isolation ratios From comparison of the data of Table 5 and of Table 9 and as summarized in Figure 2 it appears that antibiotic therapy may have had a selective effect on the bacterial flora *in persistent otitis, and apparently favored the relative increase in preva*lence of *Streptococci* particularly *Enterococci* *Micrococci* *Staphylococci* and *Cornyebacteria* remained significant throughout although their prevalences were subject to considerable fluctuation

To explore in detail the matter of change in flora composition during *treatment, the Following cultures from* individuals of Groups I II and III at 3–4 months and at 12 months were compared with the Initial cultures. These three groups were used *for the comparisons because* their Initial culture flora were similar in taxonomic character The following tabulations were made

(a) The number of species found in the Initial culture

(b) The number of species which were present in the Initial culture but not in the Following culture (at 3–4 months and at 12 months) and

(c) The number of species present in the Following culture which were not present in the Initial culture

The comparison of 3–4 months change in 22 cases showed that 79% of the species found in Initial cultures were absent in the Following cultures. In eight cases in which 12-month comparisons could be made, 88% of the species of the Initial cultures were absent in the Following cultures. At both 3–4 months and 12 months, the initial species lost were *replaced by a* larger number of different species. Since we did not have untreated cases to follow—and it would have been unthinkable to establish such a control group—the implications of antibiotic treatment in the taxonomic shift of flora must be judged from the sensitivity data presented later

As an additional check on the patterns of microbial infection a comparison was made of the flora recovered simultaneously from the left and the right ear of persons with bilateral suppurative otitis. The comparisons were graded as

(a) Identical flora

(b) Flora similar for most part

(c) Flora similar in minor part, and

(d) Flora entirely different

The results are tabulated in Table 10

These data show that in bilateral otitis, *the majority* of cases may have flora in one ear which is quite dissimilar taxonomically from the flora of the other

In general these comparative findings indicate that the microbial etiology of suppurative otitis media is not static—that once the pathogenetic chain of events is initiated and the disease is inadequately treated, consecutive changes of flora occur which, for the most part are derived from normal pharyngeal flora and to some extent from environmental contaminants.

TABLE 10 *Comparison of flora from cultures of right and left ear in bilateral otitis.*

	Initial cultures 22 cases ( )	Following cultures 46 cases ( )
(a) Identical flora in both ears	9.1	6.5
(b) Flora similar most part	36.3	30.4
(c) Flora similar minor part	22.7	39.1
(d) Flora entirely different	31.8	23.9
Total	99.9	99.9

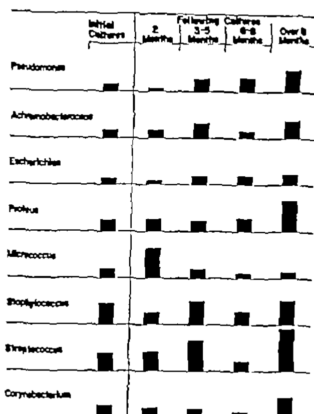


Fig 2 Comparison of fl ra components of initi l and f llowi g cultures.

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To explore in detail the matter of change in flora composition during treatment the Following cultures from individuals of Groups I II and III at 3–4 months and at 12 months were compared with the initial cultures These three groups were used for the comparisons because *their initial* culture flora were similar in taxonomic character The following tabula tions were made

sensitivity levels, initial ear cultures.

Group IV				Group V				Group VI				Group VII				Group VIII			
R	SS	S	VS	R	SS	S	VS	R	SS	S	VS	R	SS	S	VS	R	SS	S	VS
0	9	27	63	—	—	—	—	0	20	0	80	0	0	0	100	50	0	25	25
81	9	9	0	—	—	—	—	0	20	60	20	0	60	20	20	75	0	25	0
65	14	7	14	71	3	13	13	72	0	11	17	22	19	11	49	63	4	0	33
19	17	31	33	6	23	32	39	28	25	14	33	5	16	35	43	20	13	25	42
47	21	17	15	52	13	18	16	42	31	20	6	59	11	19	11	37	25	13	25
38	9	31	22	29	6	16	48	42	6	22	31	11	5	32	51	13	8	30	48
41	5	24	29	52	10	6	32	47	11	14	28	16	3	22	59	29	8	17	45
41	14	29	16	32	10	23	35	39	11	28	22	18	3	30	49	25	13	29	33
22	9	29	40	24	3	23	48	17	6	35	42	32	9	27	32	25	8	20	47
43	26	21	10	35	10	32	23	56	8	19	17	16	11	31	42	20	17	29	33
11				0				5				5				4			
48				31				36				37				24			

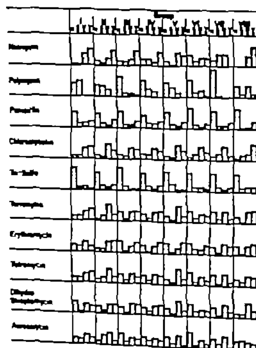


Fig 3 Distribution of antibiotic sensitivity levels—initial ear cultures.

TABLE 11 *Distribution of antibiotic*

	Group I				Group II				Group III			
	R	SS	S	VS	R	SS	S	VS	R	SS	S	VS
Neomycin	5	5	16	74	12	0	6	82	19	9	41	31
Polymyxin	37	16	37	11	41	21	35	0	68	26	6	0
Penicillin	48	16	14	21	35	11	23	29	60	1	9	30
Chloromycetin	10	18	31	38	15	12	37	35	10	12	52	25
Tri Sulfa	50	26	9	14	54	17	15	14	70	22	4	4
Terramycin	13	6	33	48	15	9	45	32	16	12	49	23
Erythromycin	24	9	12	55	25	12	20	43	33	6	21	37
Tetramycin	13	14	27	45	25	9	31	35	19	17	41	19
Di-Strep	27	12	33	28	37	8	35	20	31	12	38	19
Aureomycin	19	21	28	28	28	15	39	18	27	30	30	12
No of isolates												
Neomycin and Polymyxin	19				17				54			
Remainder	67				65				82			

ANTIBIOTIC SENSITIVITY STUDIES

The kind of antibiotic sensitivity test system used was of clinical diagnostic grade Nevertheless, a high degree of standardization in the conduct and reading of the tests was developed by the microbiological staff Consequently the test data was satisfactory for purposes of comparison of the sensitivities of flora cultivated from the cases under study

As interesting as it might be from the microbiological aspect, it is *not* possible within the scope of this paper to compare the antibiotic sensitivities of individual microbial species from case to case Since the study had a strong clinical orientation the important question to answer was "Which antibiotic or combination of antibiotics is likely to be efficacious in the treatment of the individual case as it is presented?" Further there is no reasonable basis for the designation of any one of several species found in a sample of otitis exudate as *the* etiological agent All the flora found are under suspicion Consequently the antibiotic sensitivities of the composite *flora of an otitis case are important to the* physician who must determine the agents and regimen of treatment Since it has been shown in the foregoing that flora changes with duration, it is to be expected that the spectrum of sensitivity also changes with duration The data have been tabulated to elucidate the changes that did occur The categories of sensitivity as stated *before* were *Resistant*" "*Slightly Sensitive*" "Moderately Sensitive and "Very Sensitive"

The percent distribution of grades of sensitivity of ear exudate flora

sensitivity levels, initial ear cultures.

Group IV				Group V				Group VI				Group VII				Group VIII			
R	SS	S	VS	R	SS	S	VS	R	SS	S	VS	R	SS	S	VS	R	SS	S	VS
0	9	27	63	—	—	—	—	0	20	0	80	0	0	0	100	50	0	25	25
81	9	9	0	—	—	—	—	0	20	60	20	0	60	20	20	75	0	25	0
63	14	7	14	71	3	13	13	72	0	11	17	22	19	11	49	63	4	0	33
19	17	31	33	6	23	32	39	28	25	14	33	5	16	35	43	20	13	25	42
47	21	17	15	52	13	19	16	42	31	20	6	59	11	19	11	37	25	13	25
38	9	31	22	29	6	16	48	42	6	22	31	11	5	32	51	13	8	30	48
41	5	24	29	52	10	6	32	47	11	14	28	16	3	23	58	29	8	17	45
41	14	29	16	32	10	23	35	39	11	28	22	19	3	30	49	25	13	29	33
22	9	29	40	24	3	23	48	17	8	33	42	31	9	27	33	25	8	20	47
43	28	21	10	35	10	32	23	56	8	19	17	16	11	31	32	20	17	29	33
11				0				5				5				4			
58				31				36				37				24			

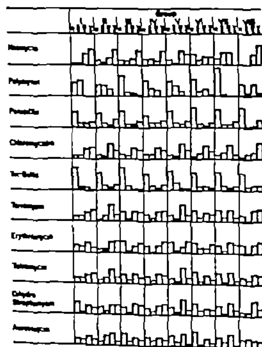


Fig. 2. Distribution of antibiotic intensitivity levels—initial ear cultures.

TABLE 12 *Distribution of sensitivity*

Antibiotic	Group I				Group II				Group III			
	R	SS	S	VS	R	SS	S	VS	R	SS	S	VS
Neomycin	4	4	38	54	16	8	24	52	10	15	20	19
Polymyxin	46	54	0	0	40	36	24	0	60	13	12	5
Penicillin	51	15	15	19	48	14	11	27	57	11	10	22
Chloromycetin	10	11	36	42	13	6	53	28	17	12	39	32
Tri-Sulfa	76	11	11	2	60	15	8	17	77	15	4	4
Terramycin	15	17	20	30	5	18	56	21	31	7	31	31
Erythromycin	23	18	32	27	13	11	37	39	39	0	22	33
Tetramycin	10	18	29	31	13	17	49	21	31	13	33	22
DIH Strep	40	6	30	24	25	11	32	32	23	7	38	32
Aureomycin	23	20	34	23	13	31	42	14	41	15	27	17
No isolated tested												
Neomycin and Polymyxin	24				25				75			
Remainder	88				71				114			

toward 10 antibiotics by case Group in relation to duration of infection (see p 11) is given in Table 11 and presented graphically in Figure 3 These data represent the composite sensitivity of the initial cultures Since the use of the proprietary medication containing them was introduced late in the study Neomycin and Polymyxin were not tested as extensively as the other antibiotics, therefore the distribution of sensitivity toward those two agents provide less reliable indices than the data obtained on the others employed in the tests

The table and graph show that none of the antibiotics tested except possibly for Neomycin, had a high degree of activity against all of the flora encountered in any one Group of cases Considering the variety of bacterial species involved in the tests, these results are to be expected The less active were Polymyxin Penicillin and "Tri Sulfa Parenthetically it is of interest to point out that Penicillin and "Tri Sulfa were the agents most often prescribed for initial treatment of the cases encountered in this study Of all of the antibiotics tested, Neomycin was by far the most active against the bacterial isolates tested against it Chloromycetin and Terramycin were moderately active against the isolates encountered in most Groups, except for Group VI Erythromycin and Terramycin activities reflected to a large extent the distribution of gram positive organisms among the Groups, particularly *Staphylococci* i e., these antibiotics scored higher in the Groups having the greater proportions of gram positive microflora The opposite was found with Streptomycin which scored better in the tests against flora with

levels— Following" culture—ear

Group IV				Group V				Group VI				Group VII				Group VIII			
R	SS	S	VS	R	SS	S	VS	R	SS	S	VS	R	SS	S	VS	R	SS	S	VS
20	20	13	46	17	3	46	34	35	17	25	23	20	40	40	0	0	0	33	67
54	26	20	0	51	34	15	0	58	17	23	2	95	5	0	0	39	11	39	11
43	16	16	25	55	14	11	20	67	12	6	15	60	10	10	20	67	3	5	25
17	16	39	28	12	8	52	28	10	20	45	25	14	23	49	14	5	18	22	55
57	16	8	19	66	23	6	5	61	15	15	9	62	16	8	14	57	13	15	15
25	9	32	34	18	7	57	18	37	13	28	22	39	11	39	11	20	2	36	42
25	4	25	46	36	6	19	39	35	20	15	30	26	8	37	29	29	2	29	40
27	11	34	28	18	8	65	10	45	11	29	15	38	8	43	11	21	15	34	30
23	11	30	36	25	7	50	18	40	15	23	22	33	7	43	17	13	13	50	24
30	21	27	22	35	15	41	9	51	10	26	13	34	18	43	5	27	30	23	20
15				35				40				20				18			
61				85				115				61				60			

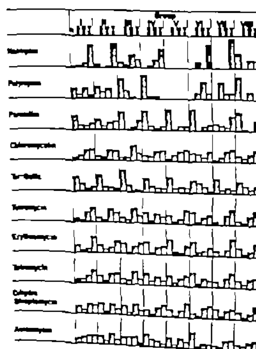


Fig 4 Distributio of antibiotic sensiti ity levels—"F llowi g" cultures, ear exudat

TABLE 13 (A) *Synopsis of comparisons of antibiotic sensitivities between initial and 3–4 month Following cultures on 22 individuals of Groups I II and III (percentage figures)*

		Neomycin	Polymyxin	Penicillin	Chloromycetin	Tri Sulfa	Terramycin	Erythromycin	Tetramycin	Di-Strep	Aureomycin
No tested		34	34	87	87	87	87	87	87	87	87
Initial cultures	R	12	69	57	15	59	14	29	19	32	21
	SS	6	35	10	16	21	15	8	13	13	30
	S	47	6	10	39	8	41	19	46	39	36
	VS	35	0	23	30	11	30	44	22	16	10
No. tested		17	17	31	31	31	31	31	31	31	31
Original spp remaining	R	18	88	52	19	84	0	0	8	29	3
	SS	6	12	22	13	16	13	13	10	8	21
	S	41	0	16	52	0	39	39	41	29	41
	VS	35	0	10	16	0	48	48	41	31	32
No tested		15	15	80	80	80	80	80	80	80	80
New species	R	13	33	50	19	61	15	27	25	31	22
	SS	0	23	8	13	6	17	13	20	9	30
	S	19	33	15	28	23	40	31	30	20	30
	VS	67	11	27	40	10	29	29	25	37	18

No. tested = number of isolates tested.

the higher proportion of gram negative bacteria *No particular trend was* apparent in the distribution of sensitivities to Aureomycin

The composite antibiotic sensitivities of the flora of the Following cultures from each Group are presented in Table 12 and graphed in Figure 4 Not many trends of sensitivity change are apparent from these data The flora of most Groups were unmistakably less sensitive to Neomycin and Polymyxin (except in Group VIII) There were, in general less marked but significant shifts toward decreased sensitivity to most of the antibiotics.

To pursue further the issue of change in antibiotic sensitivity of otitis flora with the shift in taxonomic composition and duration of infection the antibiotic sensitivities of the flora of cultures involved in the 3–4 months and 12 months comparison (see p 21) were tabulated These data are given in Tables 13 *A* and 13 *B*

In the 3–4 month comparison, no general trends in antibiotic sensitivity changes were apparent The species which were present both in the Initial and the 3–4 month Following cultures showed moderate decreases in sensitivity to Neomycin Polymyxin Penicillin, Chloramycetin a marked decrease in sensitivity to "Tri Sulfa" and a moderate increased sensitivity toward Terramycin Erythromycin Tetramycin Streptomycin and Aureomycin The new species in the 3–4 month flora of the Following cultures were

TABLE 13 (*B*) *Synopsis of comparisons of antibiotic sensitivities between initial cultures and 12 month Following cultures of Groups I II and III (percentage figures)*

		Neomycin	Polymyxin	Penicillin	Chloromycetin	Tri-Sulfa	Terramycin	Erythromycin	Tetramycin	Di-Strep	Aureomycin
No. tested		0	0	27	27	27	27	27	27	27	27
Initial cultures	R	0	0	44	11	53	15	41	19	30	30
	SS	0	0	19	19	21	4	11	11	11	19
	S	0	0	15	20	11	26	4	30	26	36
	VS	0	0	22	40	15	55	44	40	33	15
No. tested		3	3	3	3	3	3	3	3	3	3
Original spp remaining	R	33	100	67	33	67	67	67	67	0	67
	SS	0	0	33	33	33	0	0	0	0	0
	S	33	0	0	33	0	33	33	33	33	33
	VS	33	0	0	0	0	0	0	0	67	0
No. tested		38	38	38	38	38	38	38	38	38	38
"New" Flora	R	16	58	63	5	81	12	29	18	31	23
	SS	16	23	8	6	3	13	5	18	3	21
	S	16	16	11	45	11	37	37	39	35	43
	VS	52	3	16	45	5	37	29	25	31	11

No. tested – number of isolates tested.

slightly or moderately more sensitive to the antibiotics tested except for Terramycin, Erthromycin and Tetramycin where there were slight decreases in sensitivity

The 12 month comparisons were necessarily based on a small group of cases. Because all of these were cases found early in the study the Initial cultures were not tested against Neomycin and Polymyxin and sensitivity comparisons for those antibiotics were not available With regard to the other antibiotics, the species found both in the Initial and 12 month Following cultures were markedly more resistant to all except Streptomycin where there was a decided shift toward greater sensitivity This reflects the previously described trend towards persistence of gram-negative flora (see Table 9) The "New" flora showed less consistent sensitivity patterns to the antibiotics, varying from marked insensitivity to Penicillin and Tri Sulfa, to moderat sensitivity to Chloramycetin, Erythromycin and Aureomycin The data suggest that antibiotic treatment has a selective effect on the flora of chronic otitis in that those species persist which are less sensitive to the commonly used antibiotics.

Since the emergence of antibiotic-resistant strains of *Staphylococcus aureus* has been a matter of epidemiological concern in recent years, the isolates of that species were studied with particular attention to shift in anti-

TABLE 13 (A) *Synopsis of comparisons of antibiotic sensitivities between initial and 3–4 month Following cultures on 22 individuals of Groups I II and III (percentage figures)*

		Neomycin	Polymyxin	Penicillin	Chloromycetin	Tri Sulfa	Terramycin	Erythromycin	Tetramycin	Di-Strep	Aureomycin
No tested		34	34	87	87	87	87	87	87	8	87
Initial cultures	R	12	69	57	15	59	14	29	19	32	[illegible]
	SS	6	35	10	16	21	15	8	13	13	30
	S	47	6	10	39	8	41	19	46	39	36
	VS	35	0	23	30	11	30	44	22	16	10
No. tested		17	17	31	31	31	31	31	31	31	31
Original spp remaining	R	18	88	52	19	84	0	0	8	29	3
	SS	6	12	22	13	16	13	13	10	8	21
	S	41	0	16	52	0	39	39	41	29	41
	VS	35	0	10	16	0	48	48	41	34	32
No tested		15	15	80	80	80	80	80	80	80	80
New species	R	13	33	50	19	61	15	27	25	34	22
	SS	0	23	8	13	6	17	13	20	9	30
	S	19	33	15	28	23	40	31	30	20	30
	VS	67	11	27	40	10	[illegible]	29	25	37	18

No. tested = number of isolates tested.

the higher proportion of gram negative bacteria No particular trend was apparent in the distribution of sensitivities to Aureomycin

The composite antibiotic sensitivities of the flora of the Following cultures from each Group are presented in Table 12 and graphed in Figure 4 Not many trends of sensitivity change are apparent from these data The flora of most Groups were unmistakably less sensitive to Neomycin and Polymyxin (except in Group VIII) There were in general less marked but significant *shifts toward decreased sensitivity* to most of the antibiotics.

To pursue further the issue of change in antibiotic sensitivity of otitis flora with the shift in taxonomic composition and duration of infection the antibiotic sensitivities of the flora of cultures involved in the 3–4 months and 12 months comparison (see p 21) were tabulated These data are given in *Tables 13 A and 13 B*

In the 3–4 month comparison *no general trends in antibiotic sensitivity* changes were apparent The species which were present both in the Initial and the 3–4 month Following cultures showed moderate decreases in sensitivity to Neomycin, Polymyxin, Penicillin Chloramycetin a marked decrease in sensitivity to Tri Sulfa and a moderate increased sensitivity toward Terramycin, Erythromycin Tetramycin, Streptomycin and Aureomycin The new species in the 3–4 month *flora of* the Following cultures were

TABLE 13 (B) *Synopsis of comparisons of antibiotic sensitivities between initial cultures and 12 month Following cultures of Groups I II and III (percentage figures)*

		Neomycin	Polymyxin	Penicillin	Chloromycetin	Tri-Sulfa	Terramycin	Erythromycin	Tetramycin	Di-Strep	Aureomycin
No. tested		0	0	27	27	27	27	27	27	27	27
Initial cultures	R	0	0	44	11	53	15	41	19	30	30
	SS	0	0	19	19	21	4	11	11	11	19
	S	0	0	15	20	11	26	4	30	26	36
	VS	0	0	22	40	15	55	44	40	33	15
No. tested		3	3	3	3	3	3	3	3	3	3
Original spp remaining	R	33	100	67	33	67	67	67	67	0	67
	SS	0	0	33	33	33	0	0	0	0	0
	S	33	0	0	33	0	33	33	33	33	33
	VS	33	0	0	0	0	0	0	0	67	0
No. tested		38	38	38	38	38	38	38	38	38	38
"New" Flora	R	16	68	65	5	81	13	29	18	31	23
	SS	18	23	8	5	3	13	5	18	3	21
	S	16	16	11	45	11	37	37	39	35	45
	VS	52	3	16	45	6	37	29	25	31	11

No. tested = number of isolates tested.

slightly or moderately more sensitive to the antibiotics tested except for Terramycin, Erthromycin and Tetramycin where there were slight decreases in sensitivity

The 12 month comparisons were necessarily based on a small group of cases. Because all of these were cases found early in the study the Initial cultures were not tested against Neomycin and Polymyxin and sensitivity comparisons for those antibiotics were not available With regard to the other antibiotics, the *species found* both in the Initial and 12 month Following cultures were *markedly more resistant to all* except Streptomycin where there was a decided shift toward greater sensitivity This reflects the previously described trend towards persistence of gram-negative flora (see Table 9) The "New" flora showed less consistent sensitivity patterns to the antibiotics, varying from marked insensitivity to Penicillin and Tri Sulfa, to moderate sensitivity to Chloramycetin, Erythromycin and Aureomycin. The data suggest that *antibiotic treatment has a selective effect* on the flora of chronic otitis in that those species *persist* which are less sensitive to the commonly used antibiotics.

Since the emergence of antibiotic resistant strains of *Staphylococcus aureus* has been a matter of epidemiological concern in recent years, the isolates of that species were studied with particular attention to shift in anti-

TABLE 14 *Comparison antibiotic sensitivities* S Aureus *isolates Groups I II and III*

	No. tested	Initial (%) R	SS	MS	VS	No. tested	Following 4 months + Over (%) R	SS	MS	VS
Neomycin	23	9	4	65	22	13	0	8	61	31
Polymyxin	23	87	9	4	0	13	92	8	0	0
Penicillin	46	54	11	13	22	18	56	28	5	11
Chloromycetin	46	[illegible]	2	78	17	18	0	17	66	17
Triple Sulfa	46	74	20	6	0	18	83	6	11	0
Terramycin	46	4	2	59	35	18	0	6	50	44
Erythromycin	46	0	4	26	0	18	0	11	33	56
Tetramycin	46	7	0	57	37	18	0	0	56	44
Dihydrostreptomycin	46	17	1	48	17	18	11	5	67	17
Aureomycin	46	11	22	48	19	18	0	22	61	17

No of cultures in each class.

biotic sensitivity in the course of middle ear infection Table 14 presents the distribution of grades of sensitivity to nine antibiotics and Tri Sulfa of the *S aureus* isolates recovered at Initial culture of untreated cases, compared with the sensitivities of isolates recovered from cases with persistent otitis after 4 or more months of treatment. No general trend in nor drastic change of sensitivity was found in comparison of the Initial and Following cultures The sensitivities of the latter toward Tetramycin Streptomycin Aureomycin and Neomycin increased to a moderate degree Moderate decreases in sensitivity toward Polymyxin Penicillin and Chloromycetin were found In *the case of Tri Sulfa and Terramycin, both greater and less sensitivity* categories enlarged at expense of intermediate categories Certainly these data dot not indicate the induction of antibiotic resistant *S aureus* as a consequence of extended antibiotic therapy

DISCUSSION

Detailed discussions and interpretations have been given in the foregoing in conjunction with the presentation of data There remain some important *general issues which require* discussion to clarify the purpose of this paper and our conclusions

At onset of our studies we did not presume that we would define the primary etiology *of otitis media We did expect that most* of the cases of otitis coming under study would be presented at a stage when the advent of secondary pathogenic agents would have obscured the initial pathogenetic agents and events. Nevertheless, we *felt that the microbial aspects of otitis*

media, as we encountered them, would be issues of basic pathoecological importance. Furthermore, we felt that such studies could be of considerable practical importance for the stages of otitis media studied in our project are, by far the more common kinds found among the medically-indigent populations of the world, where early uncomplicated otitis media rarely receives prompt and adequate medical attention. In such areas the physician is usually confronted with suppurative otitis, a ruptured tympanic membrane and a bacteriologically-complicated infection.

Since the time of our project, great strides have been taken in the definition of th primary etiology of otitis media. In effect, the excellent work of Berglund, Grönroos and associates (12, 13, 14 and 15) have demonstrated a primary etiological role for the Respiratory Syncytial Viruses (RSV) and have shown coexisting RSV and bacterial infection in acute otitis media. Their later studies indicate that while RSV infections appear to be primary and incitatory it is the coexisting or subsequent bacterial infections that cause the more destructive and persistent pathologic events. They thus have provided scientific proof for a hypothesis long held by those who have studied and treated otitis media.

Those microbiological studies which have utilized otitis media exudate aspirated by needle puncture of the unruptured tympanum have demonstrated a rather simple bacterial flora—usually one species and more frequently a gram-positive coccus. (See Lahikainen [4] and Grönroos and associates [5].) The cases of perforating purulent otitis in our study presented a greatly complicated bacteriological picture Contrary to some generally held presumptions, the results of this study indicate that a large proportion of the kinds of flora found in chronic or recurrent exudative otitis is derived from the nasopharynx, rather than external contamination. Further there is some probability that external flora which do become established in otitis may in turn, become established in the pharyngeal flora of the diseased person. The microbiological features of otitis change in time—sometimes so rapidly that the flora of cultures taken a week apart may differ at least in part.

Persistent otitis media, on the basis of our results, appears not to be a chronic, but a recurrent disease of shifting microbial etiology One may assume certain general probabilities, such as the predominance of gram-positive cocci in the flora during the first few weeks and gradual conversion to a flora dominated by gram negative bacteria thereafter Nevertheless, in order to provide assiduous medical attention and to select the mode of treatment on a rational basis, it is highly desirable and indeed, essential, that the composition and antibiotic sensitivity of the flora present be determined culturally at successive stages in the clinical management of the case. The field physician in this study found that the bacteriological analyses, including th antibiotic sensitivity determinations, provided invaluable assistance in determining the course f clinical management and hastened the termination of infection in many cases.

The determination of the antibiotic sensitivities of a pure culture of a microorganism cannot be considered as absolute prediction of the efficacies of those antibiotics when used in the treatment of infections caused by the same microorganism. Many other factors in the pathogenesis and course of the disease may modify the effect of antibiotic therapy. Nevertheless, it is generally advisable to select antibiotics for treatment of disease according to the sensitivities of the causative organism. The results of this study indicate that the physician may have to change the antibiotic therapy in accordance with the shift in microbial flora in persistent or recurrent otitis media. It is quite noteworthy that the more commonly used therapeutic agents at the time of this study—sulfonamides and penicillin—were consistently the less active against the microbial flora which we encountered in perforating purulent otitis media. However, our tests did not include a determination of the effectiveness of various concentration levels of antibiotic or sulfonamide. Our comparisons were among components of flora with reference to a standard concentration (medium level). It must also be kept in mind that the microbiological situation of our cases was entirely different from that of early unperforated cases, such as studied by Lahikainen (4) and Grönroos and associates (5).

The ecological effect of antibiotics appeared to be considerable in that resistant flora persisted in a proportion of treated cases. There was no indication, however, that antibiotic therapy led to any substantial absolute increase in resistance of any one component of the flora. These facts again indicate that serial microbiological study of persistent cases should be carried out to determine flora and antibiotic sensitivity shifts.

In general, the etiology of otitis media is considered to be ascending infection from the nasopharyngeal tract, provoked by upper respiratory disease of viral etiology. We would agree with this concept. In addition, it is probably true that the incidence and severity of this disease among American Indians and Alaskan Eskimos is linked to their medical indigence, general poverty and status of health education. But considerations of etiology and predisposition to otitis media cannot stop with microbiological and socio-economic factors. The abnormally high prevalence of otitis media among Alaskan Indians and Eskimos, as well as among other Indian groups (16, 17 and 18) may arise, in part, from anatomical characteristics which predispose to ascending infection of the auditory tract from the nasopharynx. A number of workers have drawn correlations between occurrence of otitis and the degree of pneumatization of the temporal bone (see Lahikainen [41]). Another factor may be the relative size, length and direction of traverse of the Eustachian tube and its relation to adenoidal structures. These factors deserve rather rigorous examination among the Indian and Eskimo population, both to elucidate etiological factors and to derive ways of defining that portion of the population with the greater predisposition for otitis media. Hopefully, too, current studies on respiratory virus infections which incite otitis may lead to means of immunization to prevent the disease.

SUMMARY AND CONCLUSIONS

The bacteriological study of 130 cases of purulent, perforating otitis media among Eskimo and Indian children in Westward Alaska indicates the following

1 By their presence in otitis exudate, more than 40 species, belonging to 18 genera are linked to the etiology of bacterial otitis media. The major proportion of these species are commonly found in the pharyngeal flora of the human population studied. A minor proportion appear to be derived from external contamination.

2. Once otorrhea has been established, the microbial species associated with suppuration are usually heterogeneous, multiple and changing

3. Since the composition of microbial flora is not static in persistent or recurrent otitis, microbiological studies with antibiotic sensitivity determinations should be repeated at intervals to allow adjustment of antibiotic therapy

4 Geographic factors did not appear to have microbiological ecologic implication in this disease in the area and population studied.

5 Antibiotic therapy appeared to affect the microbiology of persistent otitis in that the more resistant bacteria were found to persist, but the induction of antibiotic resistance was not perceived.

6 The bacteriological facts alone do not fully explain the extremely high prevalence of this disabling disease among Alaskan natives. The eventual control will depend upon studied improvement of medical care and, possibly immuno-prophylaxis of incitatory viral infections.

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S U P P L E M E N T U M 259

STUDIES ON THE STRUCTURE AND INNERVATION OF TASTE BUDS

An experimental and clinical investigation

PÅL-HENRY JEPPSSON

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From the Departments of Otorhinolaryngology University of Göteborg (Head Professor G Herberts M. D) and University of Uppsala (Head Professor H Engström M. D), Sweden.

ACTA OTO LARYNGOLOGICA

SUPPLEMENTUM 259

STUDIES ON THE STRUCTURE AND INNERVATION OF TASTE BUDS

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PÅL HENRY JEPPSSON

GÖTEBORG 1969

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STRUVES BOKTRYCKERI AB
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CONTENTS

INTRODUCTION

The taste receptors in man and the higher animals are chiefly situated in special groups of cells, namely taste buds, which are located on the tongue and in the pharynx. A knowledge of the normal structure of the taste buds is of importance for the understanding of the physiology of taste and there is a comprehensive literature about these structures (Lovén 1867 Schwalbe, 1868 Hermann, 1884 1888 Ranvier 1888 Retzius, 1892 von Lenhossék, 1893/04 Gråberg, 1899 Kolmer 1910 Heidenhain, 1914 Olmsted, 1920 b) Many of these studies have been made with old-fashioned techniques and the illustrations are very often imperfect. By means of technical improvements in, amongst other things, microphotography and microscopy the possibilities of analyzing and reproducing structural details, have been improved fundamentally During the last decade a number of publications have appeared which contain illustrations that were made with the aid of electron microscopy (Engström and Rytzner 1956 a, b Trujillo-Cenóz, 1957 de Lorenzo, 1958, 1960 1963 a Murray and Murray 1960 1967 Nemetschek-Gansler and Ferner 1964 Farbman, 1965 a Gray and Watkins, 1965) In spite of these studies there is still an imperfect knowledge concerning the normal structure of the taste buds. Our knowledge of the innervation of the taste buds is also rather deficient. We are unsure of the changes appearing after injuries to the nerves belonging to them. Another still unsolved problem concerns the ability ascribed to taste buds to regenerate after transection of the taste nerves.

These problems have received increased interest in connection with the development of modern oto-surgery Every day all over the world a great number of microsurgical operations in the middle ear are being carried out. At these operations the chorda tympani, the taste nerve to the anterior part of the tongue in its intratympanic course is exposed to injury or even transected. As a result of these injuries to the chorda tympani during the operation in the middle ear disturbances arise in the taste function of those parts of the tongue which are innervated by this nerve It is therefore very common for patients to report discomfort from the tongue after a middle ear operation.

A. CLINICAL PART

I. SURVEY OF THE LITERATURE

The course of the chorda tympani in the middle ear and its function

The chorda tympani leaves the facial nerve proximally to the stylomastoid foramen and enters the middle ear through the posterior canaliculus together with the posterior tympanic artery. It runs between incus and malleus and passes above the insertion of the tendon of the tensor tympani muscle on the malleus to the anterior canaliculus in the petrotympanic fissure, where it leaves the middle ear. The intratympanic course varies. In certain cases it runs vertically and is then partly hidden by the posterior margin of the tympanic sulcus. In other cases, however, the chorda tympani has a more horizontal direction.

The chorda tympani carries afferent taste fibers from the anterior two thirds of the tongue but also contains efferent secretory fibers for the submandibular and sublingual glands. It is also questioned, whether the chorda tympani contains secretory fibers for the parotid gland (Reichert and Poth, 1933, Yannulis and Mannolidis, 1958, Rauch, 1959, Diamant and Wiberg, 1965). The nerve is attributed a motor function with innervation of the levator veli palatini muscle (Moritz, 1938, Nickl, 1950). This function, however, is denied by Zöllner (1942) and Tiedemann (1965). The chorda tympani is also considered to contain fibers of touch, pain and temperature for the anterior two thirds of the tongue (Costen et al., 1951, Tiedemann, 1965).

The taste function after operation for otosclerosis

A great number of authors discuss the frequency and effect of chorda tympani lesions in surgery for otosclerosis. It has been clearly shown experimentally (Ho, 1937, Costen et al., 1951, Eliasson and Gisselsson, 1954, Frenckner and Preber, 1934) and clinically (Krarup, 1958 b, Rice, 1963, Bull, 1965, Herrmann, 1965, Roseburg, 1966, Gerhardt and Berndt, 1967, Wiberg, 1969) that excision of the chorda tympani gives a total disappearance of the taste sense within the innervation area. The patient's subjective experience of the loss of taste, on the contrary, varies with time after the operation and perhaps also with the result of the operation. Gerhardt and Berndt (1967) among others have pointed out, that the patient's experience of the improvement of hearing is so dominating that the taste loss is completely suppressed.

Besides the loss of taste, the patients not infrequently notice a feeling of dryness in the mouth which often remains. Many items of food also are perceived to have a different taste.

The fact that the patient's discomfort is, after a time, relatively insignificant, has in all probability contributed to the fact that the experimental investigations are so few Human experiments with biopsies from the papillae of the tongue after injury to the chorda tympani have not been performed It is known that a lesion of the chorda tympani causes reduced or abolished taste function within the innervation area But, whether any form of regeneration comes about, is not shown in the literature

The above discussed problems are of great clinical interest especially since patients with bilateral otosclerosis frequently undergo operations on both sides They thereby run the risk of getting impairments of the taste on the anterior two thirds of the tongue

In experiments on animals some authors have shown regeneration of the taste buds after suture of the taste nerves (Boeke, 1917 Olmsted and Pinger 1936 Arey and Monzingo 1942 Guth 1958) But there is no evidence in the literature that anyone has carried out suture of the chorda tympani on human beings after operative injuries

With the clinical results and the experimental animal investigations as background it is necessary to discuss the possibilities of restoring the *continuity in the injured chorda tympani Reinnervation and regeneration* of the taste buds could then be induced and the function of taste would be improved

The aim of the present investigation is to study the normal structure of the taste buds and to investigate problems of importance for the understanding of the effect of injuries to taste nerves. This study has been carried out along the following lines

I *Clinical investigation*

A) To study the taste function in patients operated upon for otosclerosis *by using different tests*

II Experimental investigation

A) To study the normal structure of the taste buds in rabbits, by using light, phase contrast and electron microscopy

B) To study after nerve transection and nerve suture, the morphological changes of taste buds in rabbits.

III Discussion of methods of repairing the injured chorda tympani

Table 1 Survey of literature. Frequency and duration of postoperative taste impairment with divided chorda tympani.

Author year	Type of test	Number of cases	Without taste impairment	With taste impairment: Total number	Recovered	Persistent*
Moon Jr and Pullen, 1963	Subj.	89	50 (55%)	39 (45%)	16 (19%)	23 (26%)
Rice 1963	Subj.	53	23 (42%)	30 (58%)	17 (33%)	13 (25%)
Kersley and Gray 1964	Subj.		51%	49%	15%	34%
Ball, 1965	Subj. Obj.	126	25 (20%)	101 (80%)	61 (48%)	40 (32%)
Prades and Colls, 1966	Subj.	362	104 (29%)	258 (71%)	251 (69%)	7 (2%)
Roseburg, 1966	Subj.	39	30 (77%)	9 (23%)		9 (23%)
Gerhardt and Berndt, 1967	Subj. Obj.	39	22 (57%)	17 (43%)	16 (40%)	1 (3%)

*) more than 6 months.

Table 2. Survey of literature. Frequency and duration of postoperative taste impairment with preserved chorda tympani.

Author year	Type of test	Number of cases	Without taste impairment	With taste impairment: Total number	Recovered	Persistent
Moon Jr and Pullen, 1963	Subj.	153	125 (82%)	28 (18%)	9 (6%)	19 (12%)
Rice 1963	Subj.	64	33 (52%)	31 (48%)	21 (33%)	10 (16%)
Ball 1963	Subj.	100	56 (56%)	44 (44%)	37 (37%)	7 (7%)
Herrmann, 1965	Subj.	40	37 (92%)	3 (8%)		3 (8%)
Prades and Colls, 1966	Subj.	638	491 (77%)	147 (23%)	142 (22,2%)	6 (0,8%)
Roseburg, 1966	Subj.	100	94 (94%)	6 (6%)		6 (6%)
Gerhardt and Berndt, 1967	Subj. Obj.	276	196 (71%)	80 (29%)	4 (27%)	6 (2%)

*) more than 6 months.

In most investigations only the subjective taste disturbances postoperatively are registered after division respectively preservation of the chorda tympani Table 1 is a literature review of published follow up series in cases with divided chorda tympani Bull (1965) Gerhardt and Berndt (1967) and Wiberg (1969) are the only ones, who have performed objective tests with solutions alone or combined with electrical tests The frequency of persistent subjective taste disturbances varies considerably between 2 % and 34 % The number of cases without subjective taste disturbances varies between 20 % and 77 % average 36 % (Kersley and Gray s material excluded) These authors point out that the number of patients with subjective impairments is higher if they question them than if they put the spontaneous reports together In the table Roseburg s results are founded on spontaneously reported impairments which explains the high percentage of unimpaired taste

Even if the chorda tympani is not divided at the operation but is only stretched or suffers other trauma disturbances in the function of taste may arise and the patients subjective experiences can be both pronounced and protracted (Table 2) The number of cases without subjective taste disturbances varies between 52 % and 94 % average 75 %

The majority of surgeons consider that the chorda tympani if possible should be preserved There are however as seen from table 3 surgeons, who as a routine or in a high percentage of cases divide the chorda tympani believing that injury to the chorda tympani through stretching or partial rupture causes more pronounced postoperative impairment and a higher percentage of permanent loss symptoms (Compare table 1 and 2)

Bilateral surgery for otosclerosis is today carried out more often than in the past This means that the chorda tympani may be injured or divided bilaterally Bull (1965) reports 32 patients with bilateral division of the chorda tympani 25 patients (78 %) have persistent symptoms Besides a loss of taste a metallic taste and an aversion to certain items of food the patients have a feeling of dryness in the mouth

Clinical test methods for taste

Taste like smell has peripheral receptors belonging to the group of chemical sense organs The adequate stimulation for taste is molecules and ions in solutions

The taste impression can be classified within the following qualities sweet salty sour and bitter It is not possible to give any relation between the chemical constitution of a substance and its taste (Pfaffmann 1959)

The oldest and still the most applicable clinical test for the sense of taste is the use of solutions of varying kinds with a trial-and-error method This method is qualitative but by varying the concentration of the solution it is possible to get a semi-quantitative estimation (Bornstein 1940 b)

Table 1 Survey of literature Frequency and duration of postoperative taste impairment with divided chorda tympani

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) more than 6 months.

The sense of taste can also be stimulated in a galvanic way Sulzer (1752) and Volta (1792) have observed that a taste sensation arises in galvanic stimulation of the tongue It is however only during the last decade that methods have been worked out and apparatus constructed which are suitable for clinical use in electrical taste testing Krarup (1958 a) has constructed an apparatus the so-called electrogustometer for testing the taste function His results after the clinical application are reported in 1965 In later years a number of studies have been published on electrical taste investigations, in which Krarup s basic principles have been used (Feldmann and Maier 1959 Harbert et al., 1962 Tomita and Pascher 1964 Pulec et al., 1964 Bull 1965 Föns and Osterhammel 1968)

In stimulating the sense of taste in a galvanic way a sour to metallic taste *is created at the anode and an alkaline sensation is created at the cathode*

Comments The chorda tympani contains gustatory nerve fibers to the anterior two thirds of the tongue. The nerve can be injured at surgery for *otosclerosis* but also in connection with other operations in the middle ear for hearing improvement of for cleaning Fractures of the temporal bone and facial nerve palsy sometimes cause *damage to the chorda tympani.* The clinical investigations about taste function after surgery for otosclerosis show *that both when the chorda tympani is preserved and when it is divided* the patients perceive taste disturbances. In most studies the taste is only subjectively examined The results vary and are dependent upon the following factors the way in which the patients are questioned if they are *informed and tested preoperatively* and if they perceive hearing improvement. It is thus difficult to compare the results in the different studies. To get conclusive results it seems necessary to perform not only subjective but also objective taste examinations

Table 3 Survey of literature *Frequency of divided chorda tympani at* surgery for otosclerosis

Author and year	Number of cases	Number with divided chorda tympani
Cullford 1961	414	248 (60%)
Moon Jr and Pullen 1963	242	89 (37%)
Rice 1963	116	5[illegible] (45%)
Kersley and Gray 1964		most cases
Strong and Vaughan, 1964		*all cases*
Roseburg, 1960	608	39 (5%)
Prades and Colls, 1966	1.000	362 (36%)
Gerhardt and Berndt, 1967	315	39 (1 %)

II MATERIAL

During the years 1963 to 1967 in the Department of Otolaryngology Sahlgrenska sjukhuset, in Göteborg, 661 operations for otosclerosis have been performed. The operations have been done by different surgeons belonging to the staff of the clinic. With a few exceptions stapedectomy according to Schuknecht has been performed The chorda tympani has been divided in 70 patients or about 10 %

For the present investigation a randomized material of 141 patients has been used and divided in two groups

I Patients examined preoperatively and 1 week following the operation and then 1 6 and 12 months postoperatively This group comprises 74 patients. The chorda tympani was divided in 12 and preserved in 62 patients.

II. Patients operated upon unilaterally and examined once > 12 months postoperatively This group comprises 67 patients. The chorda tympani was divided in 22 and preserved in 45 patients

The ages ranged from 18 to 73 years with a mean of 47 years All patients have been operated upon with local anaesthesia and by a transmeatal approach. In almost every case it has been necessary to drill away bone from the posterior margin of the tympanic sulcus. The approach to the middle ear and especially to the stapes plate is often obstructed by the chorda tympani. At the operation the chorda tympani can be divided or preserved. Preserved chorda tympani includes cases where the continuity of the nerve at the operation had been preserved. This group, however comprises cases where the nerve had not been touched at all, stretched, displaced or maltreated in another way

III METHODS

Subjective taste examination

The patients have been questioned about alterations in the taste of foods, difficulties in differentiating various liquids, especially tea and coffee, and the occurrence of a metallic sensation on the tongue The patients have also been questioned about pain and numbness of the tongue and dryness of the mouth. In the present investigation changes in this respect have been defined as impaired taste.

Electrical test examination

Krarup's electrogustometer has been used in accordance with the technique applied by him. In this apparatus the stimulus intensity ranges from 0-370 μA. The intensity is recorded on a scale logarithmically divided into 23 steps Every step corresponds to 1 Electric Gust Unit (EGU)

Normally there is a great individual variation of the threshold for the electrical stimulus Krarup however considers a stimulus of 23 EGU as the limit for total loss of taste. A difference in the threshold of at least 3 EGU should be regarded as significant. As controls only the preoperative threshold value or that of the unoperated side of the tongue were used

The anode the different electrode was applied to the tongue and the cathode the indifferent electrode was applied to the wrist resting on a moistened compress. The patient was informed about the principles of the method and the procedure of testing The tongue was held softly stretched forward and the anode, a stainless steel disc with a diameter of 5 mm was applied with a light pressure to the tongue 2 regions were tested first the border of the tongue 1½ cm from the tip second 2 cm dorsal and 1½ cm lateral from the tip of the tongue The threshold value for the stimulation was determined with 3 measurements by varying the strength of the stimulus around the primary value Both halves of the tongue have been tested and compared with each other To avoid adaptation it was of importance that each stimulation did not last for more than 2 seconds and was not repeated within 30 seconds In the present investigation the post operative taste sensation has been defined as impaired when the taste threshold has increased more than 3 EGU compared to control value.

Taste examination with solutions

In testing with taste solutions, Börnstein s (1940 b) method has been applied with the following solutions and concentrations.

Solutions	Concentration in percentage		
Sucrose	4	10	40
Sodium chloride	2,5	7 5	15
Citric acid	1	5	10
Quinine hydrochloride	0 075	0,5	1

The patient was asked to put out the tongue and lean the head so that the test area was kept in a horizontal position 1 drop of the test solution was applied to the front of the tongue by a pipette It was of importance that the solution did not run backward on the tongue or down in the bottom of the mouth The patient was urged not to draw in the tongue before the taste sensation had been pointed out on a table indicated with the different taste qualities and water The stimulation time varied between 10 and 15 seconds Both the anterior halves of the tongue have been tested after each other and with increasing concentrations of the solutions The idea of the significance of impaired taste varies in different investigations. As in the electrical taste test great individual variations of the threshold values exist for the different taste solutions In the present investigation impaired taste has been defined as increased taste threshold of at least 1 concentration step in at least 2 qualities

IV RESULTS

The results of the investigations with regard to the percentage of postoperatively impaired taste in the different groups at the various test occasions is registered in table 4.

Table 4 Postoperatively impaired taste function in percentage.
Preserved chorda tympani

Type of test	Group I 63 patients				Group II 43 patients
	1 week	1 month	6 months	12 months	>12 months
Subjective	50	39	34	16	2
Electric	89	83	77	65	51
Solution	84	77	68	40	33

Divided chorda tympani

Type of test	Group I 12 patients				Group II 22 patients
	1 week	1 month	6 months	12 months	>12 months
Subjective	83	50	42	17	9
Electric*	100	100	100	100	100
Solution	100	100	100	100	100

total loss of taste

Preserved chorda tympani

The subjective taste sensation of the patients in group I i.e. patients tested pre- and postoperatively was at the examination of 1 week postoperatively impaired in 50 % of the cases. With time the frequency of taste impairment decreased. At the examination 1 year after the operation 16 % of the patients had impaired taste. In group II where the patient was tested more than 1 year after surgery only 2 % had impaired taste sensation.

By the electrical test the patients in group I showed at the examination 1 week postoperatively impaired taste in 89 % of the patients. As at the subjective taste examination the percentage with taste impairment decreased with time. But at the examination 1 year postoperatively as many as 65 % had impaired taste function. In the follow-up study for more than 1 year in group II about the same percentage (51 %) of the patients had impaired taste

The results at the examination using solutions was largely in agreement with those obtained for the electrical test, but generally the numbers with taste impairment were lower In group I 84 % of the patients showed impair

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ment of taste at the examination of 1 week and 40 % at the examination 1 year postoperatively. At the examination of patients belonging to group II impaired taste was found in 33 %.

Looking upon the patients with preserved chorda tympani from the quantitative point of view not less than 13 % showed total loss of taste as registered by the electrical test as well as testing with solutions.

Divided chorda tympani

The subjective taste sensation of patients with divided chorda tympani was at the examination of 1 week postoperatively impaired in 83 %. The frequency decreased with time. Examination of the same patients 1 year postoperatively showed that only 17 % had impaired taste. The patients belonging to group II had impaired taste sensation in 9 % of the cases.

From 1 week postoperatively and later all patients with divided chorda tympani had total loss of taste both by electrical test and by testing with solutions.

V DISCUSSION AND CONCLUSIONS

In earlier investigations the subjective impairment of taste after surgery for otosclerosis is generally the only parameter used. It is clear that this introduces considerable errors. Many factors are of importance. The percentage of taste impairment is higher if the patients are questioned than if they report spontaneously (Roseburg 1966). The percentage also increases if the patients are informed and tested preoperatively. Further, the intellectual status of the patient, the profession, the postoperative hearing gain and several other factors may influence the result. These are all in accordance with the big variations between the results of the earlier investigations based on subjective evaluation of postoperative taste sensation.

To get reliable results it is necessary to perform in addition to the subjective tests, also objective taste tests. In the present investigation electrical tests and testing with solutions have been used. However, it must be stressed that the psychophysical nature of the tests introduces errors. In testing with solutions, several other factors may influence the result. The size of the drop varies as does the size of the area on which the drop spreads. These errors are avoided when using electrical stimulation because the size of the electrode standardizes the stimulated area. According to Krarup (1965) only taste fibers are stimulated at these extremely low currents. Pfaffmann (1941) states that impulses induced by electrical stimulation run in the same fibers as those induced by solutions. Stimulation of regions without taste buds gives no sensation of taste. As strict electro-

physiological methods cannot be applied on man, the electrical test designed by Krarup must be considered as the most reliable taste test today

In many cases the question concerning the chorda tympani in stapes surgery arises whether it is better to divide than stretch, displace or maltreat this structure. It has been pointed out in the literature that the preservation of the chorda tympani gives a higher percentage of subjective taste impairment than if the chorda tympani is divided The results in group II i.e. patients analyzed more than 12 months after surgery do not speak in favor of this opinion as 9 % had subjective impairment if the chorda tympani was divided at operation but only 2 % if the chorda tympani was preserved.

Compared to other reports, presently there is a strong tendency to preserve the chorda tympani as it has been divided in only 10 % of all operations. It is interesting to see that in patients with preserved chorda tympani, not less than about 50 % had taste impairment as judged by objective testing 12 months postoperatively This means that even if we try to preserve the chorda tympani definite lesions arise in half of the patients However these lesions are graded and depending on the big individual variations the taste loss can only be expressed as the difference between the preoperative and postoperative taste threshold As the limit of total loss of taste is put at 23 EGU according to Krarup it is difficult to evaluate the results. An individual having a high preoperative threshold falls after a taste loss of a few units in the group of total loss while another individual with a low preoperative threshold having a taste loss of many units and thus a greater taste impairment is still judged as having taste. The high percentage of taste impairment (about 50 % by electrical taste test) in this material speaks in favor of the opinion that preservation of the chorda tympani when it obstructs the middle ear and especially the stapes region does not prevent taste disturbances. However the chorda tympani does not only carry taste fibers, but also secretory fibers to the sublingual and submandibular glands and according to some authors (Reichert and Poth, 1933 Yannoulis and Manolidis, 1938 Rauch, 1939 Diamant and Wiberg, 1965) also to the parotid gland. As long as only unilateral surgery for otosclerosis is performed no paramount problems arise. However today bilateral surgery is usual. Good reasons exist to be more acutely aware of the problem of the chorda tympani in connection with surgery for otosclerosis.

B EXPERIMENTAL PART

I SURVEY OF THE LITERATURE

a. The taste organ under normal conditions

The taste receptors in man and higher animals, as previously stated are situated in special cell groups taste buds, which are to be found on the tongue and in the pharynx. On the tongue the taste buds are arranged in papillae of varying appearance and it is possible to distinguish 3 different forms of papillae containing taste buds, namely the fungiform papillae the foliate papillae and the circumvallate papillae In addition there are the filiform papillae which do not have taste buds

Patton (1950) Dastur (1961) and Oakley (1967) have discussed the possibility that stimulation of so-called free nerve endings may give gustatory sensation

Embryology

The first anlage of the tongue appears in the human embryo at a length of 5 mm, as a small bulge in the mucous membrane at the bottom of the primary mouth bend The tongue muscles are of mesodermal origin and derive from the first, second third and fourth branchial arches and mainly from occipital myotomes Every branchial arch has its own nerve and because the tongue develops from a number of origins, its innervation will be complicated. The trigeminal nerve from which the lingual nerve comes belongs to the first branchial arch The facial nerve with chorda tympani goes to the second branchial arch. The glossopharyngeal nerve is the third branchial arch s nerve while the vagus nerve belongs to the fourth branchial arch (Clara 1940 Hamilton et al., 1949 Langman 1963)

The epithelium of the tongue derives from the same branchial arch as the muscles At the beginning it is cubical but later differentiates to a stratified squamous epithelium at the same time as presumptive taste buds and papillae appear The circumvallate and fungiform papillae develop first and are observed in embryos of 20 to 30 mm length Somewhat later come the foliate papillae The filiform papillae which lack taste buds, begin to develop in the embryo of 45 mm length (Hellman 1921 Clara 1940 Hamilton et al 1949 Langman 1963)

The age when the taste buds begin to develop during the embryonic stage has been investigated by a number of authors and it is reported to vary between 2 and 7 months (Lustig, 1884 Hellman 1921) Bradley and Stern (1967) report that the tongue epithelium from an embryo of 7 to 8 weeks has collections of cells with a taste bud appearance but "at 11 weeks the presumptive bud is formed

It is generally considered that the taste buds are formed from the epithelial basal cell layer in connection with fibers belonging to the taste nerves. When these nerve fibers reach the basal cell layer a differentiating process of the cells takes place. The cells elongate and form groups which resemble taste buds. Depending on how the development proceeds, these cell groups soon have the appearance of definite taste buds with pores (Hermann 1884 Griffini, 1887 Tuckerman, 1888/89 Gråberg, 1898 Marchand, 1902 Schumacher 1927 Torrey 1940 Clara, 1949 Hamilton et al 1949 Kubota and Kubota 1960 1963 Langman, 1963 Farbman 1965 b Bradley and Stern, 1967) Hellman (1921) also considers, that the taste buds are induced by nerve stimulation, but that the primary taste bud like formations, called by Hellman primitive Geschmackszwiebeln do not develop into definite taste buds but are reformed Objections have been raised against the opinion that the taste nerves stimulate the formation of taste buds. It is stated, that all epithelial tissue elements have an inborn capacity to proliferate and differentiate in various organs without the influence of nervous components. According to this later theory papillae and taste buds form first and the growth of nerve fibers should be a secondary process (Herbst, 1901 Harrison, 1904 Patzelt, 1924 McLoughlin, 1961)

The development of taste buds has also been studied by electron microscope In 1965 Farbman published an electron microscopical study on the development of taste buds on the fungiform papillae in rats and there he describes how the first beginnings of papillae appear as small epithelial bulges, when the embryo is 16 days old. On the 18th to the 21st day prenatally the nerve fibers begin to invade the epithelium and those cells, which are placed nearest the nerve structures contain a rich supply of vesicles. Farbman reports these findings in the following way "these vesicles have been interpreted as morphological evidence of an interaction between pithelial and nerve processes, an interaction which precedes differentiation of the cells into taste bud cells" At the age of 12 days the taste buds are fully developed and contain the different cell types and the taste pores.

At birth, in human beings, the taste buds are considered to be fully developed and occur in greater numbers than during later life (see p. 18)

Anatomy of the taste organ

The fungiform papillae have a clublike appearance and are seen with the naked eye Most often they have a more marked red color than the surrounding structures since the keratinizing epithelium is thinner The stroma in

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advancing age there is steady reduction of the number of papillae and also of taste buds. The fungiform papillae occur over the greater portion of the tongue's anterior two thirds during the latter part of fetal life or the earliest months of life. They are later greatly reduced in numbers.

No quantitative estimations of the number of taste buds situated on the fungiform papillae are available (Hoffmann 1875, Stahr 1902, von Skramlik, 1925, Schumacher 1927).

It is mainly the circumvallate papillae that have been the object of study first because they are easy to find on the tongue and secondly because they are few in number. In the adult, as earlier stated, taste buds occur on the lateral sides of the papillae and the inside of the wall, while in the newborn taste buds have been described also on the top of the papillae. The taste buds on the top, atrophy or disappear as a result of the continual wear of the tongue against the palate when sucking, swallowing and crying. Individual variations with regard to the number of papillae, their size and shape cause great difficulties when estimating the number of taste buds during different periods of life. Von Wyss (1870) calculated the number per papilla at 400, Krause (1876) at 2500 and Gräberg (1899) at 100 to 150.

Through Heiderich's (1906) and Arey's et al. (1935) investigations it has become evident that the taste buds are passing a progressive involution. Heiderich (1906) could, by serial sectioning of the circumvallate papillae from individuals between 0 and 20 years of age, estimate the number of taste buds to an average of 248 per papilla. This figure is remarkably constant for all ages. In the work of Arey *et al.* (1935) papillae were also serially sectioned with the following result: in the age group 20 to 70 years there is an average of 208 taste buds per papilla but in the extreme age group 74 to 85 years there are only 88 taste buds per papilla.

Physiological behaviour

Several earlier authors (Ranvier 1888, Hermann, 1888, von Lenhossék 1893/94, von Ebner 1897) have, in their investigations of the structure of the taste buds, observed the occurrence of a varying number of leucocytes within the taste buds. This observation led to the thought that a steady degeneration of cells in the taste buds is taking place. However, this degeneration is partly compensated for by simultaneous renewal.

Further support for this hypothesis has been obtained through Hermann's (1888) discovery of mitoses in the lower part of the taste buds. Kolmer (1910), Retzius (1912) and Heidenhain (1914) also supposed that a continuous transformation is taking place in the cells of the taste buds.

It is, however, through the studies of Beidler et al. (1960), Beidler (1961, 1963), Beidler and Smallman (1965) and Robbins (1967) on animals definitely proved that the cells in the taste buds pass a continuous process of degeneration and renewal. Beidler et al. injected colchicine, a mitosis inhibitory substance, intraperitoneally into rats and then killed the animals and

the papillae consists of connective tissue nerves and blood vessels In many places the stroma projects into the epithelial layer whereby secondary papillae are formed The number of papillae vary individually and also with age As a rule the younger an individual is the greater is the number of papillae They are scattered over the anterior two thirds of the tongue but are especially numerous near the tip and the anterior margin of the tongue The number of taste buds in the papillae varies between 3 and 12 (Parker 1922 Bloom and Fawcett 1908) Fungiform like papillae which do not contain any taste buds have also been described (Schumacher 1927 Maximov and Bloom 1952)

The foliate papillae in man are rudimentary while those of some animals, such as rabbit and rat are well developed (Hellman 1921 Schumacher 1927) In mammals the foliate papillae are situated on the lateral sides of the tongue at the border between radix and corpus linguae and form 4 to 8 parallel ridges with furrows between

The taste buds occur on the lateral sides of the ridges, but there also are ridges which have no taste buds and this has been considered to be a sign that the papillae are in a state of regressive development The stroma in these papillae is formed by connective tissue, rich in fat and lymphoid structures (Stahr 1902) The secondary papillae of the foliate papillae are often particularly regular and well developed In the peripheral areas, the furrows are as a rule more shallow

The circumvallate papillae 3 to 12 in number are located directly in front of the terminal sulcus and are arranged in a V like formation The size of the papillae can vary but externally they have the same characteristics and are composed of a central papilla separated by a furrow from the surrounding wall The taste buds are situated partly on the lateral side of the papilla partly on the inside of the wall facing the furrow (Schumacher 1927 Maximow and Bloom 1952 Bloom and Fawcett 1968) In newborns sometimes there are taste buds on top of the papillae (Hoffmann 1875 Tuckerman 1889/90 Gråberg 1898 Jurisch 1922 Schumacher 1927)

Solitary or smaller groups of taste buds can be found embedded in the epithelium on various places in the oral cavity or the pharynx Thus, Hoffmann (1875) and Parker (1922) found taste buds on the soft palate above the uvula In spite of serial sections however von Ebner (1897) Patzelt (1924) and Cairns (1955) could not find any taste bud like structures in this area

Ponzo (1905) Patzelt (1924) and Märk (1940) have found taste buds on the posterior wall of the pharynx on the glossopalatine arch and on the epiglottis.

In the fetus Patzelt (1924) has found taste buds in the orifice to the esophagus Schinkele (1942) and Burkl (1953/54) have described taste bud like structures in the middle part of the esophagus.

Taste buds seem in general to be fully developed at birth and with

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Taste buds seem in general to be fully developed at birth and with

advancing age there is steady reduction of the number of papillae and also of taste buds. The fungiform papillae occur over the greater portion of the tongue's anterior two thirds during the latter part of fetal life or the earliest months of life. They are later greatly reduced in numbers.

No quantitative estimations of the number of taste buds situated on the fungiform papillae are available (Hoffmann 1875 Stahr 1902 von Skramlik, 1925 Schumacher 1927)

It is mainly the circumvallate papillae that have been the object of study first because they are easy to find on the tongue and secondly because they are few in number. In the adult, as earlier stated taste buds occur on the lateral sides of the papillae and the inside of the wall while in the newborn taste buds have been described also on the top of the papillae. The taste buds on the top, atrophy or disappear as a result of the continual wear of the tongue against the palate when sucking, swallowing and crying. Individual variations with regard to the number of papillae, their size and shape cause great difficulties when estimating the number of taste buds during different periods of life. Von Wyss (1870) calculated the number per papilla at 400 Krause (18 6) at 2500 and Gråberg (1890) at 100 to 150

Through Heiderich's (1906) and Arey's et al. (1935) investigations, it has become evident that the taste buds are passing a progressive involution. Heiderich (1906) could by serial sectioning of the circumvallate papillae from individuals between 0 and 20 years of age, estimate the number of taste buds to an average of 248 per papilla. This figure is remarkably constant for all ages. In the work of Arey et al. (1935) papillae were also serially sectioned with the following result in the age group 20 to 70 years there is an average of 208 taste buds per papilla but in the extreme age group 74 to 85 years there are only 88 taste buds per papilla.

Physiological behaviour

Several earlier authors (Ranvier 1888 Hermann, 1888 von Lenhossék 1893-94 von Ebner 1897) have, in their investigations of the structure of the taste buds, observed the occurence of a varying number of leucocytes within the taste buds. This observation led to the thought that a steady degeneration of cells in the taste buds is taking place. However this degeneration is partly compensated for by simultaneous renewal.

Further support for this hypothesis has been obtained through Hermann's (1888) discovery of mitoses in the lower part of the taste buds. Kolmer (1910) Retzius (1912) and Heidenhain (1914) also supposed that a continuous transformation is taking place in the cells of the taste buds.

It is, however through the studies of Beidler et al. (1960) Beidler (1961 1963) Beidler and Smallman (1965) and Robbins (1967) on animals definitely proved that the cells in the taste buds pass a continuous process of degeneration and renewal. Beidler et al. injected colchicine a mitosis inhibitory substance intraperitoneally into rats and then killed the animals and

studied the *taste organs* histologically They found very many cells with mitotic division around the taste buds, but none inside them The highest number of cells with mitotic division was reached after 6 hours and after about 12 hours it was normal again Parallelly a degeneration of the cells inside the taste buds took place After 8 hours there was degeneration in only a few taste buds but after 48 hours there were degenerative changes to be found in the majority of taste buds

Through these experiments it has been shown that the cells in the taste buds of rabbits undergo a degenerative process. In order to show that renewal of cells also is taking place Beidler et al injected labelled tritiated thymidine, which was "picked up by cells during their DNA synthesizing period prior to mitotic division" (Leblond et al., 1959) The tongue was prepared sectioned and radio-autographed later with varying time intervals after the injection These investigations show that the cells, which have divided in the periphery of the taste buds continuously wander to the center A number of the cells never reach the center but degenerate before they reach it.

Beidler et al. estimated the life span of the cells to be about 250 ± 50 hours in rats These experiments according to Beidler and others have shown that there is a continuous renewal of cells in the taste buds. De Lorenzo (1963 b) carried out similar investigations in rabbits and got the same results.

Fine structure of the taste buds

The taste buds consist of tightly placed ovoid bodies with slender cells Their long axis generally lies at right angles to the surface layer of the epithelium on the papilla They vary in size and also in form in different animal species as well as in different animals of the same species Sometimes they are nearly round, sometimes oblong At the base, which reaches *the germinative layer of the epithelium nerve fibers penetrate* The upper pole of the taste bud reaches the surface of the epithelium and is marked by an excavation the taste pit, in which a number of slender microvilli are located. The taste buds mostly lie separately but sometimes they are more complex and may then have 2 or more pores

Since Lovén s and Schwalbe s (1867) discovery of taste buds in higher animals a great number of publications have come out which deal with their structure and innervation

Lovén (1867 1868) mainly studied the circumvallate papillae in calves *but also in man* *Taste buds or taste bulbs* which Lovén proposed they should be called are, according to him composed of 2 cell types suppor ting or covering cells and taste cells The latter are considered to be a special end organ and should constitute a direct continuation of the sensory nerve

Schwalbe (1867 1868) who investigated taste buds from among other animals, horse ox and sheep, also described 2 cell types under the same

name as Lovén. The taste cell ends in the pore in a hair like formation Besides this taste cell Schwalbe found even another type called "Stab-zellen" which reaches the pore without the hair-like formation.

Both Lovén and Schwalbe in their first works, believed that the covering or supporting cells were placed peripherally in the taste buds and surroun ded the centrally situated sensory cells. Schwalbe, however reported (1887) that the supporting cells could occur inside the taste buds

Ranvier (1868) described partly the inner and partly the outer supporting cells in the taste buds.

In 1888 Hermann showed that covering cells occur intermingled with the sensory cells and that there is yet another supporting cell, the basal cell, in the lower part of the taste bud.

Von Lenhossék (1893/94) could not verify basal cells in his examinations of taste buds from a rabbit s tongue. On the contrary he found 4 different forms of supporting cells peripherally situated in the taste bud and con sequently not intermingled with the sensory cells. Only 1 type of sensory cell occurs and this is not to be understood as a continuation of the nerve.

Gräberg (1899) who studied taste buds from human tongues, observed 1 form of sensory cells and 3 different types of supporting cells, which, with regard to their position, were called central, peripheral and basal. The 2 first named supporting cells have the same structural forma tion and constitute the same type of cell, but with different localization in the taste bud. The basal cell, however differs from the others from a structural point of view Gräberg, however could not clearly characterize the structural differences

Many authors have earlier proposed that it is possible to differentiate between supporting and sensory cells. Kolmer (1910) for example described fibrils in the supporting cells. Between these "extremes" in the structure there were transitional forms, which, through their not so characteristic patterns, were difficult to group. The occurrence of these transitional forms could, according to Kolmer be an expression of a process, in which the cells were in different stages of function and development.

Retzius (1912) and Heidenhain (1914) agreed with Kolmer's opinion and further pointed out that taste buds should be regarded as a more uniform tructure

Ultra tructure of the taste buds

After the basic histological investigations of the structure of the taste buds at the end of the nineteenth and the beginning of the twentieth centuries, no extensive work ha been published, dealing with structural problem, until during the last decade when the electron microscopical reports have come Kolmer (1927) has, however in "Handbuch der mikroskopischen Anat mie des Menschen" given a fairly thorough survey of the structure of ta te buds.

In 1956 Engström and Rytzner with a short interval published 2 electron microscopical works on the ultrastructure of the taste buds in the rabbit In these works which are the earliest published 2 cell forms were described where one of them was slender with a little cytoplasm and the other more voluminous with a broad cytoplasm containing granules and vacuoles All the cells reach to the taste pore and there end in a number of finger like projections villi. In spite of certain differences in the structure of the cells, the authors considered however that it was not possible to differentiate between sensory cells and supporting cells, but pointed out that it was quite possible that the cells could pass over from one form into another during their life-cycle

Trujillo-Cenóz (1957) also described only 1 type of cell in his electron microscopic study on the taste buds in rabbit

De Lorenzo (1958 1960 1963 a) on the contrary distinguished sensory cells and supporting cells in the rabbit The former which extend from the base of the taste bud to the taste pit have a dark nucleus with dense granular cytoplasm and end in the taste pit in microvilli Supporting cells have a more diffusely granular nucleus and less dense cytoplasm with granules and vacuoles These cells do not reach to the taste pore

Like de Lorenzo Iriki (1960) Nemetschek-Gansler and Ferner (1964) found 2 well defined types of cells in the taste buds of rabbits with the same appearance as those described by de Lorenzo

In an electron microscopy study on the taste buds in rats Farbman (1965 a) described from a morphological point of view 4 separate cell types namely peripheral cells, basal cells, together with type I and type II cells The peripheral cells are least differentiated and are considered to be precursors of the other types These cells lack contact with intraepithelial nerve structures From a morphological point of view the basal cells are similar to the peripheral but have contrary to the latter contact with nerve structures and in addition contain vesicles The type I cells, the most numerous, were considered to constitute the taste receptors. As type I cells, the type II cells are also situated centrally in the taste buds and have contact with the intraepithelial nerve structures Type II cells contain an abundance of vacuoles and vesicles and were considered to be significant for the formation of the taste pore

The most thorough studies of the taste buds ultrastructure have been carried out by Murray and Murray who in 1960 reported an investigation in monkeys where the taste buds from the circumvallate papillae were studied The structure of the individual cells can vary quite considerably but they are only of 1 type namely gustatory Microvilli occur in the pore but they are not as conspicuous as in the rabbit Murray presented in 1961 the result of electron microscopic studies of the taste buds of rabbits 2 types of cells with gustatory function were described partly more numerous slender dark cells with granules in the apical part and partly more

rarely occurring light vacuolised cells. Both cell types terminate in microvilli in the taste pit. In 1967 the result was published of the continued studies in a work where 200 taste buds from the foliate papillae in rabbits were studied. It was confirmed, that there exist 2 cell types. As in the work from 1961 the cells are described as "light" and "dark". They both contain fibrils in the cytoplasm, but, there are more in the "dark" cells. Both cell types terminate in villus-like projections into the taste pit. The "light" cells also have centrioles with rootlets but no kinocilium, which is considered as evidence that the cells have gustatory function. The "dark" cells are supporting "with possibly a gustatory function as well".

Innervation

The course of peripheral taste nerves has ever since the beginning of the nineteenth century been the object of interest from a clinical as well as experimental point of view.

Bellingeri (1818) was the first who described that the chorda tympani contains taste fibers, but as early as 1822 Magendie stated that the trigeminal nerve carries taste fibers. These early publications, however, are only the *beginning of a discussion of the role of the facial and trigeminal nerves as* origin of taste fibers.

Claude Bernard (1843) had, through clinical studies of patients with facial nerve palsy and by experimental investigations in dogs, noted that injury to the chorda tympani gave taste disturbances. The chorda tympani, however, was by Bernard considered to have a motor function. By stimulating the chorda tympani in human beings, who after various *forms of surgical approaches to the middle ear or as a sequel to chronic otitis* have had the nerve exposed, Duchenne (1850) and Blau (1879) created taste sensation on the anterior two thirds of the tongue. Further support for the view that the chorda tympani carried taste fibers from the anterior parts of the tongue comes through investigations of Gozot and Carells (1839) and Biffi and Morganti (1846). Today there exists unanimous agreement that the chorda tympani mainly carries taste impulses from the anterior two thirds of the tongue.

Regarding the further course of the taste pathways, some of the most important opinions will be discussed in the following section.

The chorda tympani follows in its most peripheral course the lingual nerve. In the infratemporal fossa it leaves this nerve and continues alone toward the base of the skull, passes the middle ear and joins the facial nerve in the Fallopian canal, as a rule proximal to the stylomastoid foramen (Gray 1953, Jeppsson 1967). The taste fibers follow the facial nerve to the geniculate ganglion, after which, via nervus intermedius, they reach the nuclei in tractus solitarius (Lussana, 1869; Dixon, 1897; Cushing, 1903; Lewis and Dandy, 1930; Carmichael and Woollard, 1933; Zotterman, 1935; Weingarten and Gloning, 1954; Mackenzie, 1955; Krarup, 1958 b; Feldmann

and Maier 1959 Carco, 1959 Pulec et al., 1964 Krarup 1965 Motta et al 1964 *Pascher and Fischer 1968*)

The taste fibers from the chorda tympani can also run via the various branches of the trigeminal nerve in a central direction. Some authors (Erb, 1875 Gowers, 1897 Tato and Sebastian 1955 Motta et al 1964) have reported the following pathways as probable for the taste fibers. From the geniculate ganglion the taste fibers go to the sphenopalatine ganglion via the great superficial petrosal nerve and further through the maxillary nerve to the semilunar ganglion

Others (Gowers 1897 Ziehl 1889 Krause 1895) on the contrary considered that the taste fibers run from the geniculate ganglion to the otic ganglion via the small superficial petrosal nerve and then in the mandibular nerve to the semilunar ganglion

While the majority of authors have considered the chorda tympani as the nerve which supplies the anterior part of the tongue others (Eulenburg 1871 Godskesen 1888 Luciani 1911 Tschiassny 1950) contend that the glossopharyngeal nerve alone carries the taste fibers in a central direction from the whole tongue Thus the taste fibers should run in the following way via the chorda tympani to the geniculate ganglion and further via the small superficial petrosal nerve over anastomoses to the tympanic plexus and Jacobson s nerve to the glossopharyngeal nerve

The posterior third of the tongue is generally considered to be supplied by the glossopharyngeal nerve

Taste buds situated in the pharynx and larynx are innervated by the vagus nerve.

The gustatory afferent pathways ipsilaterally lead to nuclei in tractus solitarius where the secondary gustatory neuron is situated (Blomquist and Antem 1965 1967) From tractus solitarius they however continue in the opposite ascending medial lemniscus to the arcuate nucleus of thalamus

It is mainly through electrophysiological studies either by the preference method or by recordings from various levels in the taste area it has been possible definitely to elucidate the taste pathways (Blum et al 1943 Patton et al 1944 Andersson and Jewell 1957 Benjamin and Akert 1959 Oakley and Pfaffmann 1962 Bradley 1963)

There are very few clinical reports on tumours in the thalamus (Adler 1935 Gänshirt 1950) or injuries (Weingarten and Cloning 1954) with taste disturbances The earlier opinion was that the cortical representation of taste and smell is situated in the same area at uncus and gyrus hippocampi Through Börnstein s work (1928, 1940 a) however it is agreed that the central projection of taste is at the lower portion of gyrus pre and postcentralis Börnstein s result has been verified by electrophysiological investigations. In these experiments the chorda tympani was stimulated and the evoked potentials in the cortical centers were studied (Bremer 1923 a b Patton and Amassian 1952 Benjamin and Pfaffmann 1955 Cohen et al

1937 Landgren, 1957 Benjamin and Akert, 1959 Benjamin and Emmers, 1960 Landgren et al., 1967) These studies showed that the central projection of taste is not separately located, but it is within the tactile projection area of the tongue There also are some investigations with the preference method and these also support the opinion that the taste center is situated around gyrus pre- and postcentralis (Blum et al. 1943 Bagshaw and Pribram 1953)

Shenkin and Lewey (1944) Weingarten and Gloning (1954) reported taste disturbances in patients with cerebral injuries or tumours within the supposed taste centers.

Penfield and Boldrey (1937) could create taste sensations in patients, in whom they stimulated cortical areas of gyrus pre and postcentralis.

It can thus be stressed that the taste buds on the fungiform papillae on the anterior two thirds of the tongue are innervated by the chorda tympani and that those on the circumvallate papillae and the foliate papillae on the posterior third of the tongue are innervated by the glossopharyngeal nerve. In man, and also rabbit the innervation from both the nerves is homolateral. Chorda tympani is considered, however to have a certain overlapping on the tip of the tongue (Zander 1897 Wiberg, 1967 1969)

Intragemmal nerve structures

In the earliest studies concerning the innervation of the *taste buds*, the sensory cells were considered to be a direct *continuation* of the nerve penetrating the taste buds (Lovén, 1867 1868 Schwalbe 1867 1868 Fusari and Panasci 1889/90) By nerve staining technique the innervation pattern could be charted in another way and the earlier opinion refuted (Retzius, 1892 von Lenhossék, 1892/93 Arnstein 1893) *Their results* are in the main, in agreement with our present opinion about the innervation of the taste buds (Kolmer 1927 Kadanoff 1965 Bloom and Fawcett, 1968) Just below the taste buds is a *tortuous* nerve plexus and from this run branches, partly to the inside of the taste buds, intragemmally partly to the epithelium between the taste buds, intergemmally The latter fibers also can envelop the taste bud and are then named perigemmal. The nerves divide repeatedly in their course towards the surface of the epithelium and often exhibit small terminal enlargements Nerve fibers have been observed running intragemmally as far as to the region of the taste pit

The contact between the sensory cell and the nerve has, through electron microscopy studies been shown to occur in a synaptic way (Engström and Rytzner 1956 a, b Trujillo Cenóz, 1957 de Lorenzo, 1958, 1960 Iriki, 1960 Murray and Murray 1960 1967 Nemetschek-Gansler and Ferner 1964 Gray and Watkins, 1965 Farbman, 1965 a) Gray and Watkins (1965) the authors who most thoroughly studied the synaptic regions of the taste buds, point out, however that "membrane specialisations differ from the membrane thickenings of other types of synapse Presynaptic dense projec-

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were transported away by phagocytes. The place of the cover-cells was taken by epithelial cells.

In earlier reported works, after the transection of the glossopharyngeal nerve, changes in the taste buds were found. Later however Baginsky (1893, 1894) repeated the experiment but could not see any changes of a degenerative nature or a disappearance of taste buds, despite an observation time of between 3 and 37 days. He pointed out that on the side of the tongue where the function of the nerve was the same as in normal animals, changes could be observed of the same nature which earlier authors had thought to be dependent upon nerve injury. Microscopical examinations of the nerves in the peripheral regions, showed pronounced degenerative changes in the ganglionic cells and the protoplasm contained an abundance of granules. According to Baginsky's opinion however these changes could not be assigned any greater value.

The inside of the tongue is innervated by 2 nerves, the glossopharyngeal nerve and the chorda tympani. All earlier experiments refer to the excision of the glossopharyngeal nerve. There are, however, a number of studies, in which the chorda tympani has been cut off selectively or in its common course with the lingual nerve. In the year 1917 Boeke reported an investigation where he had divided the lingual nerve in hedgehogs and saw degeneration of the papillae with taste buds on the ipsilateral anterior half of the tongue.

By the excision of the lingual nerve in dogs, Olmsted (1921) showed that the taste buds disappeared through a degenerative process. Phagocyting leucocytes were observed in the taste buds. The breakdown products were also presumed to be pushed out through the taste pore. Epithelial cells replaced the taste buds and in the germinative layer there appeared a considerable number of mitoses. Olmsted (1922) also carried out a selective excision of the chorda tympani in dogs and got the same result. In studies of the innervation of the tongue muscles in cats, Langworthy (1924) reported that after excision of the lingual nerve no taste buds could be observed on the anterior parts of the tongue.

With the intention of mapping out the innervation areas of the various taste nerves in rats, Whiteside (1927) carried out excision of the glossopharyngeal nerve and the chorda tympani. He found that excision of the glossopharyngeal nerve only caused a total disappearance of taste buds in the posterior furrows of the foliate papillae, while in the anterior furrows a number of intact taste buds could be observed. However, if he at the same time carried out division of the chorda tympani on the same side he got complete disappearance. In rats, then, contrary to rabbits, the foliate papillae's anterior portion is innervated by both the glossopharyngeal nerve and the chorda tympani. The circumvallate papillae are innervated bilaterally by the glossopharyngeal nerve, while the fungiform papillae are supplied by the chorda tympani. The degeneration of the taste buds started

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Ganglion cells have been found under the tongue papillae (von Lenhossék 1893/94 Merkel 1917 Kolmer 1927 Iwayama and Nada 1967 a, b Bloom and Fawcett 1968) The possibility has been brought up that the taste buds have an autonomic innervation (Kolmer 1927 Desgranges, 1966)

b The taste organ after transection of gustatory nerves

By means of earlier experimental investigations it has been found that the receptor organs for taste, the taste buds degenerate after severance of the *nerves which belong to them.*

The first investigations were carried out by von Vintschgau and Hönigschmied (1876) who in 2 rabbits excised the glossopharyngeal nerve on one side of the neck and after 5 months killed the animals The foliate and circumvallate papillae were dissected out fixed in 1 % osmic acid and then examined Macroscopically there were no certain changes The microscopic examination revealed that the normal number of taste buds were found on the unoperated side, while in the operated side practically all the taste buds had disappeared In the one animal the furrows in the foliate papillae were more shallow on the operated side than on the unoperated side.

In 1880 von Vintschgau published a further work on rabbits in which he had carried out the excision of the glossopharyngeal nerve and killed the animals at various intervals after the operation. On examination no changes in the taste buds were observed within the first 24 hours, while clear changes were seen *already after the first 2 days Certain taste buds* situated more deeply seemed bigger than others and so-called "Deckzellen" furnished with granules had begun to lay themselves against the epithelial cells The changes in the sensory cells could not be evaluated During the 2nd and 3rd day there were also seen changes in the more superficially situated taste buds and all the forms were *transitory between normal and* wholly disorganized taste buds The degenerative process continued and after 7 days a considerably reduced number of taste buds existed After 3 weeks no certain taste buds could be found Von Vintschgau s impression was that 'Deckzellen had been transformed to epithelial cells He had not come to any *decision regarding the disappearance of the taste cells.*

Griffini (1884 1887) Drasch (1887) Ranvier (1888) Sandmeyer (1895) and Meyer (1896) by means of similar experiments confirmed the results of earlier investigations But contrary to von Vintschgau and Honigschmied they saw a complete disappearance of the taste buds Ranvier *felt that the sensory* cells degenerated and the breakdown products

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a de-differentiation or metamorphic transformation process occurs and imply that the so-called "Deckzellen changes into common epithelial cells. Whether the taste cells are changed or not cannot be stated with certainty Some authors (Ranvier 1888 Olmsted 1921 Whiteside 1927 Guth, 1957) have found proof that the taste buds disappear through a degenerative process. Ranvier (1888) has given the earliest and most detailed description of this process. The cells in the taste buds are disorganized, they degenerate and are phagocyted by leucocytes. Some of the break down products are also pushed out through the pores, which are considered to be the last structures to disappear The taste buds are replaced by epithelial cells. Mitoses have been observed in the germinative layer

According to Olmsted (1920 a) May (1925) and Torrey (1934) there is a neurohumoral substance in cat-fish which constitutes the trophic factor between nerve and taste bud. The authors divided the taste nerves in the cat fish and got degeneration of the taste buds. The course of events was not similar to those in warm-blooded animals The taste buds were intact for some days and then rapidly degenerated in one day The authors felt that these events proved their hypothetical assumption of a neurohumoral substance This substance occurs in the peripheral nerve stump and is consumed within a certain period of time. The time however is influenced by the temperature and the length of the peripheral nerve stump

Whiteside (1927) and Guth (1957) have discussed the hypothesis of the neurohumoral factor in their reports of experiments on rats. These authors point out that the course of degeneration is quite different. The degenerative process goes n from the first day after the excision and up to a week until it is finished. In conclusion it can be stated that there is a fundamental difference in the relation between nerves and taste buds in warm-blooded and cold-blooded animals.

c. The taste orga after suture of gustatory nerves

There are only a few reports about the regeneration of taste buds after injuries to the taste nerves The problem in the studies of regeneration has as a rule been whether the taste buds can reform after reinnervation of only gustatory or only non-gustatory nerves.

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Guth (1957) also used rats as experimental animals in his study Bilateral excision of the glossopharyngeal nerve was carried out and histological investigation of the circumvallate papillae undertaken As shown by many earlier authors, a degeneration of the taste buds occured The changes which appeared in the epithelium were also studied by Guth He found that the epithelium over the circumvallate papillae was reduced to a third or more of its original thickness. This reduction was evenly distributed over the whole surface of the papilla and not only in the area where taste buds previously had been found

Already in 1927 Whiteside had shown that the circumvallate papillae in rats was innervated by the glossopharyngeal nerve from both sides. With the support of these results Guth (1963) carried out unilateral and bilateral excision of the glossopharyngeal nerve to study the effect of partial and total denervation Guth kept calculations of the number of taste buds per section and determined the thickness of the epithelium both 7 and 35 days after the operation Unilateral excision of the glossopharyngeal nerve caused a statistically significant reduction of the number of taste buds by 12 % In determining the number of cells per taste bud there was a reduction up to 25 % Bilateral excision caused a complete loss of taste buds *The epithelium was also considerably reduced The same values were* found in calculations carried out 7 and 35 days postoperatively Bilateral excision gave a total loss of taste buds within 7 days and also more noticeable atrophy of the epithelium on the operated side as compared with the intact side. These findings would indicate that the taste buds are bilaterally innervated and every nerve fiber supplies a number of cells. Beidler (1963) injected alcohol into the middle ear of rats with the intention of injuring the chorda tympani As early as 4 to 8 hours later the taste buds became smaller and after 96 hours there were only a few taste cells but no taste pores After 7 days all the taste buds had disappeared

Olmsted (1920 a) May (1925) and Torrey (1934 1936) divided the nerve to "the barbel of a cat fish Ameiurus which contains taste buds and got complete degeneration after 10 to 12 days

From the above comparison of experimental investigation by transection of the taste nerves in mammals it is clear that after a certain time a total loss of taste buds occurs both in mammals and fish The way in which this takes place, has been discussed by some authors others only confirm that it has taken place Von Vintschgau (1880) and Meyer (1896) consider that

a de-differentiation or metamorphic transformation process occurs and imply that the so-called "Deckzellen" changes into common epithelial cells. Whether the taste cells are changed or not cannot be stated with certainty. Some authors (Ranvier 1888, Olmsted, 1921, Whiteside 1927, Guth, 19) have found proof that the taste buds disappear through a degenerative process. Ranvier (1888) has given the earliest and most detailed description of this process. The cells in the taste buds are disorganized, they degenerate and are phagocyted by leucocytes. Some of the break down products are also pushed out through the pores, which are considered to be the last structures to disappear. The taste buds are replaced by epithelial cells. Mitoses have been observed in the germinative layer.

According to Olmsted (1920 a), May (1925) and Torrey (1934) there is a neurohumoral substance in cat-fish which constitutes the trophic factor between nerve and taste bud. The authors divided the taste nerves in the cat fish and got degeneration of the taste buds. The course of events was not similar to those in warm blooded animals. The taste buds were intact for some days and then rapidly degenerated in one day. The authors felt that these events proved their hypothetical assumption of a neurohumoral substance. This substance occurs in the peripheral nerve stump and is consumed within a certain period of time. The time however is influenced by the temperature and the length of the peripheral nerve stump.

Whiteside (1927) and Guth (1957) have discussed the hypothesis of the neurohumoral factor in their reports of experiments on rats. These authors point out that the course of degeneration is quite different. The degenerative process goes on from the first day after the excision and up to a week until it is finished. In conclusion it can be stated that there is a fundamental difference in the relation between nerves and taste buds in warm-blooded and cold-blooded animals.

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portion of a non-gustatory nerve is joined to a gustatory distal portion Boeke (1917) has on hedgehogs and Olmsted and Pinger (1936) on dogs, shown taste buds after anastomosis between the hypoglossal nerve and the lingual nerve while Arey and Monzingo (1942) on dogs, and Guth (1958) on cats did not obtain new formations of taste buds in spite of long periods of observation In all the investigations it is pointed out that immediately postoperatively there is a total disappearance of the taste buds

Oakley (1967) in rats carried out end to-end anastomosis between the lingual and glossopharyngeal nerves. After about 15 weeks electrophysiological recordings were performed on the reinnervated nerves By chemical stimulation of the receptor organ a summated nerve response resembling that of the distal anastomosis portion is obtained The author draws the conclusion partly that a reinnervation has occurred and partly that a regeneration of the taste buds has taken place No histological examination is reported however

Griffini (1887) and Whiteside (1926) after experimentally created local injury to the tongue where the innervation is intact show that taste buds develop on regenerated taste papillae

II MATERIAL AND ANIMAL EXPERIMENTS

Rabbits have been used as experimental animals. They have well developed bilateral foliate papillae on the posterior lateral area of the tongue. These papillae are distinctly delimited and contain a large number of taste buds, which are innervated by the glossopharyngeal nerve (N IX) In order to produce degeneration of the taste buds transection of this nerve is carried out and regeneration is initiated by suturing the divided nerve

A large number of taste buds from other animals notably monkeys have been studied in order to compare the normal structure of different animals The results of the studies of the other animal species is not included in the following report but has been used as a comparison during the course of this work

The total number of rabbits used was 90 and of these 33 have been used for the analysis of the normal structure 38 were used for the study of degeneration in connection with nerve severance and the other 19 rabbits comprise the group containing the sutured glossopharyngeal nerves The weight of these rabbits at the beginning of the experiment was between 1.2 kg and 2 kg

Preparation of the foliate papillae

In the beginning of this study the animals were killed by an air embolus. The tongue was then immediately removed and the region with the foliate

papillae was excised and divided into suitable pieces for fixing. It was apparent however that the above method did not give good results so the procedure was changed. Instead of killing the animal immediately it was anaesthetized with mebumal-sodium (6%) and the corner of the mouth clipped up to give a better view of the back of the tongue. The jaws were held apart with a clamp and the area with the foliate papillae became fairly easily accessible. The papillae were then excised and divided into suitable pieces for fixing. In most cases the papillae were bent apart from one another and a number of incisions were made at right angles and also parallel with the long axis of the papillae. In this way the solution penetrated more rapidly down into the submucous tissues.

The specimens were, as a rule, fixed in veronal-buffered 1.5 % osmic acid solution for 2 hours, followed by a washing in physiological saline. They were then dehydrated in increasing concentrations of alcohol and propylenoxide. The specimens were then embedded in epoxy resin (Epon 812) or acrylate.

In 5 rabbits during the later part of the investigation, the specimens were fixed in a phosphate-buffered 2.5 % glutaraldehyde solution (pH 7.5). The solution was perfused through the common carotid artery for 10 minutes. It was possible to verify that the solution had passed into the tissue by the appearance of a yellow color in the mucous membrane in the oral cavity. When the perfusion was finished, the papillae were excised in the same way as described above. After 6 to 8 hours the specimens were post fixed in veronal buffered 1.5 % osmic acid solution and then dehydrated and embedded in epon.

In 7 cases the specimens were fixed and stained according to Maillet's modified zinc-iodine method (ZI staining, Engström et. al. 1966). The specimens were fixed 8 to 10 hours and rinsed and dehydrated before embedding. These embedded specimens were sectioned with glass knives in an LKB Ultrotome and then the sections were studied in light and phase contrast microscopy (Wild research microscope M 20 with camera). The film material: Kodak Tri X Pan 120 was used. The same microtome was used for preparing the sections for electron microscopy. The sections which were examined in the light and phase contrast microscope are stained in a solution of paraphenylendiamin (Estable-Puig et al., 1965). The sections for electron microscopy are stained in uranyl acetate and lead citrate and examined in a Siemens Elmiskop IA.

Transection of the glossopharyngeal nerve

The transection of the glossopharyngeal nerve was performed on rabbits anaesthetized with mebumal-sodium (6 %) injected either intraperitoneally or through a marginal vein at the ear. In order to reduce bleeding in the operation area, xylocain-exadrin (0.5 %) was injected locally. The operation was in all cases carried out on the right side of the neck with the most sterile



Fig 1 Lateral view of the neck of a rabbit after skin incision The stylpharyngeal muscle has been divided and the course and relation to other structures of the glossopharyngeal nerve (N IX) can be seen. Note the small branch (arrow) of the glossopharyngeal nerve Low power magnification.

conditions possible When a suitable depth of anaesthesia had been attained the fur was cut and incision was made just below and parallel with the lower jaw Through blunt dissection through the muscles on the neck which are against the base of the skull the glossopharyngeal nerve was identified The nerve was followed peripherally where it runs medially and somewhat cranially to the hypoglossal nerve About 1 cm below its departure from the jugular foramen on the base of the skull a branch of the glossopharyngeal nerve leaves and runs parallel to the main nerve in a peripheral direction (Fig 1) The division of the nerve was carried out about 5 mm below the base of the skull and 2 to 3 mm of the nerve was excised It was of the greatest importance that the bifurcation of the nerve be dissected out before the excision In this way no branch could be left by performing the excision in too peripheral a manner The operation was carried out under a microscope and very slender instruments were used Generally no appreciable bleeding occured during the operation The skin was sutured with nylon thread and no postoperative wound infection was noted Those animals which were supposed to survive for a longer time were put into their cages the rabbits increase in weight in the normal way

Suture of the glossopharyngeal nerve

The procedure of the experiment of nerve suture was identical with the foregoing until the glossopharyngeal nerve was dissected out. In order to get a better view of the nerve and a greater area in which to work the stylopharyngeal muscle was divided. The nerve division was proximal to the site of branching. The operation was carried out under a microscope and generally under 25x magnification. This division must be done with careful dissection so that the circulation around the nerve will not be disturbed. The free stumps were separated to make certain that all the fibers were sectioned. Thereafter the stumps were brought together and sutured with a silk suture (Ethicon 8/0). The divided muscle and skin were sewn up. No postoperative infection was noted. The animals grew and increased normally in weight.

At the end of the experiment, the animals were killed by a plan previously decided upon, and the foliate papillae were excised and prepared in the manner described above.

III. RESULTS

a. The normal structure

As pointed out earlier the furrows in the peripheral parts of the foliate papillae region are shallow while the central region has deeper furrows. In order to get uniformity in the material investigated and to be able to correctly appreciate both the normal and pathological structures, in the main, the central parts within the papillae have been examined. The aim has been to work with corresponding areas in each of the papillae.

The foliate papillae

The foliate papillae consist of a number of ridges or lamellae and furrows. These furrows contain the taste buds. The area with papillae can vary in f rm an size. The surface of the papillae is covered with stratified squamous epithelium. The epithelium as a rule projects down in the stroma of the ridges like two wedges, which after sectioning at right angles to the direction f the lamellae gives the appearance of pseudopapillae. The stroma in the papillae consists of connective tissue, fat, nerves and blood vessels. Centrally in every lamella there is a sinusoid like vessel (Fig. 2)

In the epithelium, the taste buds (Fig. ") are situated with the top or the taste pit, toward the furrow and the base toward the stroma of the papilla. The taste buds are situated only on the surface opposite the furrow and no taste buds on top of the lamellae were observed. Within the central parts of the papillae ridges occasionally occur which are partly but not wholly lacking ta te buds. However the absence of the taste buds is more common in the peripheral areas.

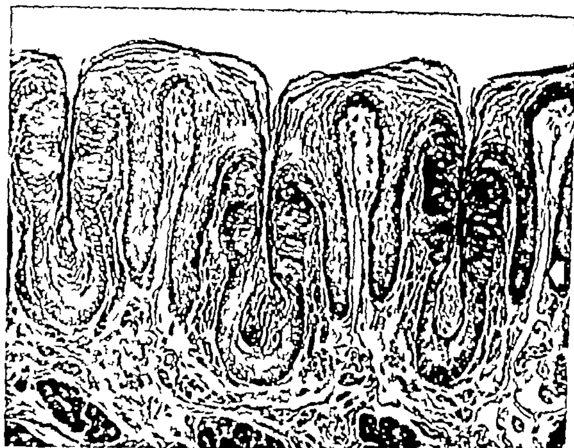


Fig 2 Central part of a foliate papilla with ridges and furrows. The taste buds are situated in the epithelium against the furrows. Nerve profils appear not only subepithelially but also deeper in the core of the papilla. Centrally the ridges contain a sinusoid vessel (arrow). Note the epithelial projections into the core of the papilla giving a pseudopapillary appearance. Phase contrast microscopy 100 x

The taste buds

The taste buds have a relatively uniform shape and appearance in the mouth In light and phase contrast microscopy they appear as lighter (Fig 3) oviform formations in the somewhat darker and denser epi thelium The cells of the taste buds generally reach from the basement membrane to the small taste pit through a taste pore which opens into the surface of the tongue. This implies that the individual cells are rather high and slender while those in the central part are nearly cylindrical On the contrary those situated on the periphery of the taste bud often appear in the histological section to be sickle-shaped The taste bud is surrounded by the squamous epithelial cells of the tongue which are rich in tonofibrils and contain large numbers of desmosomes These desmosomes generally make it easy to distinguish "gemmal" and "nongemmal epithelial cells The taste pore is seen as an opening in this dense layer of squamous epithelial cells At the base of the taste bud a number of unmyelinated nerves penetrate. These nerve fibers form a rich plexus of chiefly unmyeli

All figures are from specimens of rabbit fi ed i osmic cid (1,5 %)

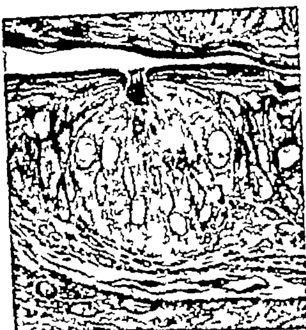


Fig. 3. Taste bud, normal, with the taste pit at the top and the nerve entrance at the base. The nucleus of the light cell is round and that of the dark cell is oblong. A few osmiophilic granules appear under normal conditions. Note that the greater part of the nuclei are situated in the lower half of the taste bud. Phase contrast microscopy 780 x.

nated fibers just below the taste bud. Some of them come from the perigemmal areas situated between the taste buds.

In rabbits, the cells within the taste buds vary quite considerably in structure and there is great difficulty in differentiating the various cell types from one another. Sometimes it can even be difficult to distinguish neural elements from the taste bud cells. This applies above all to those nerve fibers reaching the proximity of the pore.

It has not, in this investigation, been possible to decide whether or not perigemmal cells can be transformed to gemmal. It is clear however, after studying a large number of taste buds, that many different varieties of cell forms, of cell density and of cell inclusions can occur in the taste buds of the rabbit.

In light microscopy taste bud cells usually appear lighter than the surrounding squamous epithelial cells. Within the individual taste buds the cells vary in form and shape in a manner which encourages classification into light and dark cells. The same difference appears in phase contrast microscopy when studying specimens embedded in epon and stained with paraphenylendiamin solution. The distribution of light and dark cells varies considerably. It seems that cell degeneration and cell breakdown affect the the light cells first. It can now be established that through this investigation it has not been possible to distinguish 2 completely different forms of cells in the taste buds. However, all variations and transitions have been observed between narrow, dark cells with slender nuclei, rich in chromatin and light cells with rounded nuclei. An extensive contact between

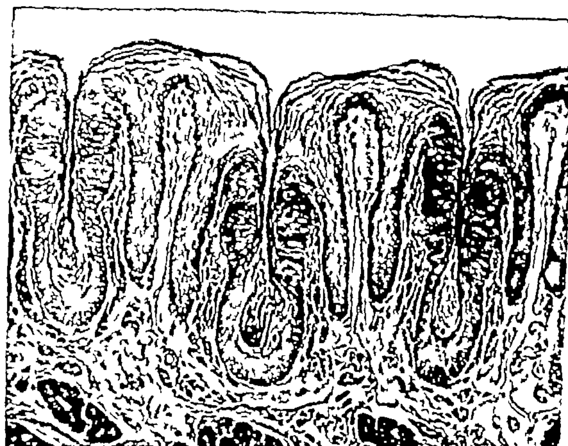


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All figures are from specimens of rabbits fixed in o mic acid (1,5)



Fig. 5 Detail from fig. 4. The supranuclear part of dark cell with a solitary microvillus (rrow) The cell contains centriole (*Ce*) with cross-banded rootlets downwards. Electron microscopy 32 000 x.

penetrating nerve fibers and all types of cells brings about further difficul ties in judging whether a cell has a gustatory or supporting function.

In the following part the intention is to give an account of the epithelial element of the taste buds by first describing the dark cells. This will be followed by a description of the light ones together with cells of the transitional type with widespread degenerated cytoplasmic pictures.

The dark cells at the apical surface have a brush of microvilli which projects from a rather coarse neck" Not all the microvilli belonging to the dark cells extend from a common neck" Many of the villi protrude directly from the surface of the cell and sometimes they can also be solitary (Fig. 4 and 5) The microvilli are surrounded on their free surface



Fig 4 Apical part of a ta te bud with the ta te pit The dark cells (D) contain n merous osmi philic gran les nd the light cells (L) many mall vacuoles Th pical part f the cell ends in microvilli (MV) of different shape nd siz Note the centriol (arrow) with it cross banded rootlets. Electron microscopy 10 000 x



Fig. 7 Upper part of a taste bud. The dark cell (D) centrally contains well developed microvilli extending from the neck portion and branching. The attachments between the cells are complex. Electron microscopy 18 000 x.

fibrillar elements of corresponding caliber are often seen infranuclearly in the cells.

The dark cells near the taste pit contain long microtubules frequently with a curved shape. These are most often spread diffusely between the thin filaments. The cytoplasm of the dark cells has a further type of fibrillar structures, namely microfilaments which appear in bundles traversing the



Fig 6 Some microvilli extending from the surface of a cell into the taste pit The microvilli are bordered by a double (triple) outer membrane The outer of these membranes is often provided with a fine brush like surface structure (arrow) Electron microscopy 63.000 x

by a double membrane (Fig 6) It cannot be established but it seems probable that the most developed microvilli are provided with fine macromolecular surface differentiations The villi and its neck contain particularly fine fibrillar structures arranged in a parallel way They extend from the villi and from the "neck in the supranuclear part of the cells (Fig 7) Whether the fibers reach even further down is not clear but



Fig. 7. Upper part of a taste bud. The dark cell (D) centrally contains well developed microvilli extending from the neck portion and branching. The attachments between the cells are complex. Electron microscopy 16 000 x.

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Fig 9 Detail from fig 8. The dark cells contain numerous osmiophilic granules. Centriole (Ce) Multivesiculated body (arrow) Electron microscopy 13,000 x.

From the lower part the centrioles project cross-striated rootlets toward the cent r of the cell It is impossible to determine how deep these rootlets xtend into the taste bud. The filaments extending from the microvilli often run in a direction opposite the centriole

Rather densely packed mitochondria of varying size with a round to an al form occur plentifully in the cytoplasm of the dark cells. The cell contains a moderately richly developed rough endoplasmic reticulum and some multivesiculated bodies.

Adjacent cells, dark as well as light, stand in contact with one another through desmosomes, which occur rather sparsely and are mainly found in the upper region of the taste buds. Plasma membranes to adjacent cells are



Fig 5 Part of the apical half of a taste bud The attachments between the cells are very complex Numerous vacuoles are seen in the light cell (L) and only very few in the dark ones. Bundles of filaments extend downward from the villi to the apical part of the cell. Even centrally filaments (arrow) are seen Nerve structure indicated by N Electron microscopy 8,000 x.

cytoplasm (Fig 8 and 9) Close to the nucleus, these microfilaments are more densely arranged (Fig 10) They chiefly appear in the supranuclear region but can often be found in the infranuclear area

In the apical part near the taste pit the dark cell cytoplasm contains many homogeneous osmiophilic granules varying in size (Fig 4 and 5) These granules appear chiefly in the supranuclear region but can be found even in the basal part of the cell

The centrioles with their characteristic appearance are outlined as a homogeneous dense substance around a lighter center (Fig 5 and 9) They are situated quite near the upper margin of the cells, in the region between the nucleus and the pore and often at right angles to the axis of the villi



Fig. 9. Detail from fig. 6. The dark cells contain numerous osmiophilic granules. Centriole (Ce). Multivesiculated body (arrow). Electron microscopy 13,500 x.

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Fig 10. Nucleus (Nu) and the supranuclear region of a light cell in a taste bud. The cytoplasm contains bundles of filaments arranged more densely close to the nucleus. Many mitochondria (M) also are seen. Likewise the cytoplasm contains special vesicles with a darker central part. Nerve indicated by N. Electron microscopy 13,500 x

also connected to one another by complicated infoldings (Fig 11) which give a considerable increase to the cell surface These infoldings are most pronounced in the upper region of the cells

The light cells are also provided with microvilli on their apical surface. It seems as if these villi are less developed than those which belong to the dark cells (Fig 4) The villi often extend directly from the cell surface and a "neck" corresponding to that on the dark cells is missing The microvilli in the light cells are also membraned and have a fine fibrillar inner structure which continues down into the cells

The endoplasmic reticulum of the light cells is as a rule different from that in the dark cells (Fig. 4 and 8) The cytoplasm contains a large number of vacuoles and a few osmiophilic granules of up to 0 5 μ in size Correspon ding inner structure is often observed in the endoplasmic reticulum in taste bud cells after nerve transection to a considerably greater extent than before Whether the presence of vacuoles and osmiophilic granules in taste buds of



Fig. 11. Attachments between cell. A. Junctional complexes between light and dark cells in the taste bud.
B. and C. Desmosomes. Fine fibril (tonofibrils, within the cytoplasm converge at the desmosomes. Note the bands between the membranes. Electron microscopy. A. 12,500 B. 27,000 C. 140,000 x.

normal animals is an expression of cell degeneration cannot be decided with certainty.

The light cells contain the same forms of microfilament as the dark ones but to a considerably lesser degree. Mitochondria, rather densely packed, ribosomes and multivesiculated bodies occur though sparsely in the cytoplasm of the light cells.

In spite of investigating a large number of taste buds from the foliate papillae on rabbits, it has not been possible to find centrioles in the light



Fig 10 Nucleus (Nu) and the supranuclear region of a light cell in a taste bud. The cytoplasm contains bundles of filaments arranged more densely close to the nucleus. Many mitochondria (M) also are seen. Likewise the cytoplasm contains special vesicles with a darker central part. Nerve indicated by N Electron microscopy 13,500 x

also connected to one another by complicated infoldings (Fig. 11) which give a considerable increase to the cell surface. These infoldings are most pronounced in the upper region of the cells.

The light cells are also provided with microvilli on their apical surface. It seems as if these villi are less developed than those which belong to the dark cells (Fig 4) The villi often extend directly from the cell surface and a neck corresponding to that on the dark cells is missing The microvilli in the light cells are also membraned and have a fine fibrillar inner structure which continues down into the cells

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Fig 12 Cross secti ned nerve l undles situated subepithelially in the papilla Both myelinated and unmy linated nerve fibers are seen Von l l ner s glands in the l wer right corner Phase contrast microscopy 800 x

cells Whether this is caused by technical problems cannot yet be decided There should of course be some centrioles, even in these cells.

Other cell forms

Among the cell forms which cannot be classified as light and dark cells it is possible to distinguish in the main 2 categories One of these has a nucleus with a chromatin density and a form and also an endoplasmic reticulum with a shape which compares closely to that of the dark cells The cell has microvilli of varying length and number generally the villi extend from a neck shaped structure. Filaments and microtubuli occur but are not so regularly shaped These cells have granules of similar appearance to the dark cells and sometimes vacuoles also Mitochondria and a dense mat of ribosomes accompany this cell variant As a rule there are distinct centrioles in the supranuclear portion of the cell

The other cell type has an appearance most like the light cell and it seems to be a further development of this type The cytoplasm here gives the impression of being in a degenerative stage *This cell form which is* found centrally in the taste bud is characterized chiefly by its rich supply of vacuoles of a definite dimension in the cytoplasm In general microfilaments and mitochondria appear very sparsely Both kinds of cells are in *complex connection* with the cells and the nerve structures.

Nerves

When investigating a specimen fixed in osmic acid and stained with paraphenylendiamin solution in light and phase contrast microscopy no



Fig. 13. Nerv[illegible] fiber (N) close t[illegible] [illegible] termination to a dark cell. The dark cell nucleus indicated by N[illegible] J[illegible]nctional complex (arrow[illegible]) Electron microscopy 13 500

detailed information of the distribution of the intragemmal nerve structures and th[illegible]ir relation to the cells is revealed. With this staining the nerves appear as light, round to oval formations between the cells. In the upper half of the taste bud they occur sparsely but it is possible to find a solitary nerve close to the taste pit. The lower half and especially the region of the nerve entrance in the taste bud, on the contrary is provided with a large number of nerve elements. The intragemmal nerves are unmyelinated, while those which are below the taste buds and deeper subepithelially are myeli nated. The myelin sheath appears as a dark round ring around the axon and in this fixing and staining, it is easily distinguishable (Fig. 12)

In electron microscopy it is possible to study the ultrastructure *of the* nerves and the contact with the cells In some cases, however it can be very difficult to differentiate the cells of the taste buds *from* those *of* the nerve structures This applies particularly to those nerves situated in the proximity of the pores. Both structures are provided with membranes but



Fig. 14. Nerve ending (NE) sparsely granulated in contact with a cell. The cell contains many granules similar to synaptic vesicles just at the contact zone. Electron microscopy 38.000 x

the nerves are devoid of ribosomes. The nerves divide in their intragemmal course repeatedly and end in club-like swellings, or boutons.

The intragemmal nerves are of varying calibers and contain neurotubuli, which in specimens sectioned longitudinally have a nearly parallel course. In addition the nerves contain a few rather densely packed mitochondria (Fig. 13).

In this study typical contacts of a synaptic nature have been observed between the different cells and the nerve endings. Within other sensory organs which have been studied by the research group most frequently large numbers of synaptic vesicles and granules appear. The rabbit's taste buds contain however only sparse numbers of synapses, but for these regions they have typical vesicles and granules.

The nerve endings are, as pointed out earlier, club-like formations and seem from a morphological viewpoint the same as in other sensory regions like the ear or the eye, to be of 2 different kinds. One of these has only a few



Fig. 15 From the basal part of two djacent taste buds close to the nerve entrance A richly granulated bouton (NE) can be seen. It contains typical synaptic vesicles. Other nerves (N) mitochondria and multivesiculated bodies (arrows) are also visible. Electron microscopy 20 000 x.

synaptic vesicles often with a diameter around 500—600 Å. While the presynaptic side, i.e. the sensory cell side, generally contains special synaptic organelles. Such granular presynaptic differentiations are found as "synaptic bars (Smith and Sjöstrand, 1961 Spoendlin and Gacek, 1963) The other type of nerve ending is richly provided with synaptic vesicles and appears to be of presynaptic type. This would indicate a centrifugal conductivity in this type of nerve ending (Fig. 14 and 15)

On some occasions in this investigation contact has been observed between different types of nerve fibers indicating neuro-neuronal contacts. As in synaptic areas, these regions have a rather opaque appearance.

In this connection a further observation must be pointed out. On a number of occasions in the taste buds of the normal material, nerve structures have been observed very near to the taste pit. It has not been possible to see any characteristic synaptic structures in the contact zone between the nerve and the surrounding cell.



Fig 14 Nerve ending (NE) sparsely granulated in contact with a cell The cell contains many granules similar to synaptic vesicles just at the contact zone. Electron microscopy 30.000 x

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Fig. 17 Nerves immediately below the base of a ta t bud with my linated nd unmyelinated fibers The myelin is distinctly lamellated. Not the outer (black arrow) nd inner (white arrow) mesaxons Schwann cell nuclei (SC) Electron microscopy 20.000 x.

AZ-staining

In this type of staining, not only the nerve structures appear but also the cell elements The staining of the cells varies however It seems as if those cells designated "light are stained first. They appear as bulky formations with large, round nuclei (Fig. 20) which are a little lighter than the cell in general. Those cells which are called dark are stained more irregularly and not so distinctly (Fig. 21) Both types of cells extend from the base of the taste bud to the taste pit where they continue into microvilli.

In the study of the nerve structures, thick sections (15—20 μ) have been prepared but in spite of this it has not been possible to follow the course of the nerve complexes from the deeper area lying in the papillae among musc



Fig 16 Part of a cross sectioned nerve below the taste bud This nerve has been stained by the Maillet technique This impregnation has given a considerable density to the epineurium (E) and to the myelinated nerves (My) while the unmyelinated nerves are surrounded by Schwann's cell (SC) cytoplasm only NZ staining Maillet modified zinc iodin method Electron microscopy 10 000 x

As pointed out above the nerves running subepithelially are partly myelinated partly unmyelinated and of varying calibers (*Fig 16*) In the core of the papillae between the glandular structures and muscles, the nerves form large bundles In electron microscopy *the myelin lamellae* appear very clear Their numbers can be counted and their course followed from the outer to the inner mesaxon (Fig 17)

The unmyelinated nerves are situated close to or completely enclosed in Schwann's cell (Fig 18) The axon is in this way surrounded by the double membrane from the latter

Ganglionic cells with myelinated and unmyelinated nerves have on some occasions been observed in the subepithelial tissue (Fig 19)

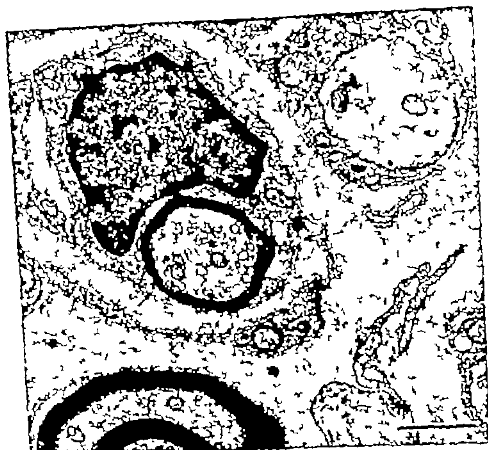


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N

Fig. 18. Myelinated (My) and unmyelinated (N) nerve fibers. Electron microscopy 90,000 x.

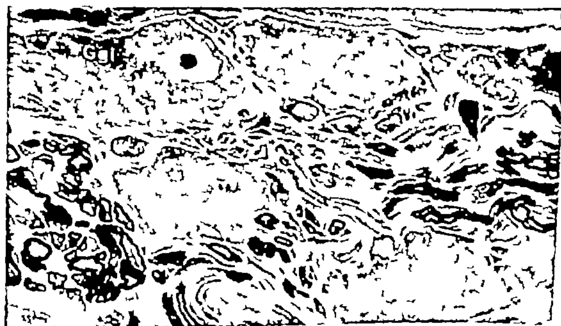


Fig. 19 Ganglionic cells (Ggl) with myelinated (bla k) and unmyelinated nerve Phase contrast microscopy 900 x.



Fig. 20. Part of foliate papilla with differently stained cells i the ta t bud. Furrow indicated by arrow. NZ-staining. Maillet's modified zinc-iodine method. Light microscopy 750 x.



Fig 21 Differently stained cells in the taste bud NZ staining Maillet's modified zinc iodine method Light microscopy 1510 x.

les and glandular structures to the most superficial subepithelial regions under the taste buds There is always a rich nerve plexus running just under the epithelium along the furrows (Fig. 22) From this plexus a large number of branches occur almost at right angles to the surface They appear not only in the region where the taste buds are situated, but also at the base of the furrows (Fig. 23) These nerves bend near the surface of the epithelium and run parallel with it. Whether these fibers terminate as free nerve endings" has not been possible to decide in this study In the region beneath the taste buds a nerve plexus is situated and from it nerve fibers run partially intragemmal and partially inter and perigemmal The nerves running outside the taste buds divide repeatedly and reach the surface of the epithelium in the furrows Bead like swellings often occur on these nerve fibers (Fig 22) In their course intragemmal nerve fibers also divide between the cells and a number of these nerves reach the region just under or in the taste pit.



Fig 22. Deepest part of furrow from foliate papilla. The subepithelial nerve fibers have tortuous course. Subgemmally is a nerve plexus (n.pl.) giving off nerves both intragemmally and inter- and perigemmally. Some of the cells in the taste buds are stained black. XZ-staining, Maillet's modified zinc iodine method. Light microscopy 360 x.



Fig. 23. The individual nerves course in the epithelium perpendicular to the free surface where they turn off. XZ staining, Maillet's modified zinc iodine method. Light microscopy 360 x.



Fig 21 Differently stained cells in the taste bud NZ staining Maillet's modified zinc iodine method Light microscopy 1510 x

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b. The structure after nerve transection

The rabbits were sacrificed at varying intervals after transection of the glossopharyngeal nerve, as shown in table 5

Table 5 The number of rabbits and their survival time after transection of the glossopharyngeal nerve.

Survival time in days	1	2	3	4	5	6	7	10	14	30	90	180	270
Number	2	2	5	5	2	2	7	3	2	2	3	1	2

Control animal. In order to exclude the possibility that the surgery caused disturbances in the continuity of the glossopharyngeal nerve 1 animal was killed 7 days after the operation, when only the nerve was dissected out. The taste buds at the foliate papillae showed no structural changes nor did the subepithelially coursing nerves.

Macroscopic findings
Before killing the rabbits, the region with the foliate papillae was inspected via the operation microscope and the operated and unoperated sides were compared. Animals which were examined within 30 days after transection of the glossopharyngeal nerve showed no certain observable changes. 1 animal, however with a survival time of 10 days had an ulcer centrally in the papilla on the operated side and there the furrows and ridges were missing. After 90 days survival the papilla on the operated side seemed paler than on the unoperated, but the normal surface structure was preserved.

Microscopic findings
After transection of the glossopharyngeal nerve, structural changes occurred in the taste buds on the *ipsilateral* papillae and in the subepithelial nerve structures. The process, which was progressing, was studied by light, phase contrast and electron microscopy As soon as *24 hours* after the nerve transection there were easily visible changes, not only in the cells of the taste buds but also in the nerves running subepithelially There are often difficulties in following the course of events in detail but in the following paragraphs, the main features of the process will be described. In studying the changes of the structures on the operated side, comparison has always taken place with the unoperated and the normal side.

The number and size of the taste buds was unchanged in the first *2 days* after transection. The light cells which normally contain a few osmiophilic granules, had an abundance of them in the cytoplasm. The granules increased in size and gradually clumped together These granules were well



Fig 21 The same vesicular structures as seen in fig 10 A nerve (N) containing some granules, resembling synaptic vesicles are also seen. Electron microscopy 21 000 x

Special cytoplasmic structures in taste bud cells

On several occasions we have observed large numbers of intracytoplasmic granules in taste bud cells and even in their nuclei These inclusions have a varying diameter (Fig 24) Each granule has a denser center and a distinct outer membrane There are several regions indicating that the granules are more numerous close to the nerve endings than in the rest of the cells This could indicate a connection of synaptic importance However these granules are considerably larger than ordinary dense core synaptic vesicles and it is quite possible that they have a totally different significance Thus we have discussed if they could have some relation to viruses. Virus infections in the taste buds of human beings have been discussed recently by Blatt and Freeman (1968)



Fig. 27 The same specimen as in fig. 26 but here the nucleus is partly visible. The nuclear (N) membrane is diffuse but the membrane of the cell (arrow) is still distinctly visible. Electron microscopy 22,500 x.

demarcated but irregularly shaped. In some parts they contained a filamentous whirl-like inner structure, and in others they had a homogeneous appearance. The cytoplasm also contained a large number of vacuoles and gave the impression of a coarse spider's web. The fibrillary structures, both of tubular and microfilamentous character were still intact. The mitochondria were in this stage not so densely packed. The cell and nuclear membranes were intact but the nucleus had already at this stage of degeneration an irregularity in structure and the chromatin showed a tendency to clotting. The cytoplasm in the dark cells now contained a few vacuoles and the granules normally occuring in the dark cells, had increased

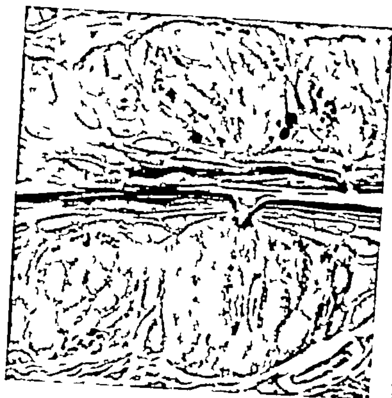


Fig 25 Taste buds from an animal sacrified 3 days after transection of the glossopharyngeal nerve The size of the taste buds and the numbers of cells is unchanged in comparison with the normal side The osmiophilic granules appearing under normal conditions have increased in size and number Phase contrast microscopy 800 x

Fig 26. Part of taste b d from n animal sacrifled 1 dav aft tra section f the glosso-pharyngeal nerve A an in lication of degen rati n, the cyt pla m co tai both vacuoles and vesicles of vario ize Electron microscopy 20 000 x



Fig. 29 Central part of taste bud from an animal sacrificed 3 days after transection of the glossopharyngeal nerve. The cytoplasm contains lysosomes and degeneration products of different size and shape. Electron microscopy 20 000 x.

times appeared in normal taste buds (Fig. 26 and 27) Only a few not so densely packed mitochondria appeared (Fig. 28) The microvilli seemed to be intact. The dark cells showed no additional obvious changes on the third day compared with the second day (Fig. 29)

The size and number of the cells in the taste buds had so far been unchanged compared with those of the normal side, but between *the 4th and 5th day* after transection of the nerve the taste buds were more slender and had sometimes a somewhat irregular shape. The pore still remained, but all the cells did not reach it. The microvilli cannot be distinctly distinguished. This change in their outline was dependent upon the fact that



Fig 23 Central part of a taste bud from an animal sacrificed 3 days after transection of the glossopharyngeal nerve The *nuclear membranes* of both light and dark cells are not smooth any longer Possible degeneration of some mitochondria (arrows) Electron microscopy 8500 x.

in size and were to be found uniformly in the cytoplasm The pore with the microvilli were unchanged

The structural changes which had occurred were most obvious in the light, most peripherally situated cells As time proceeded after the transection of the nerve more changes appeared however also in centrally situated light cells Between *the 2nd and 3rd day after the transection* there were pronounced changes of the same appearance as those just described in all light cells and in the majority of the dark cells (Fig 25) The osmiophilic *granules had however increased in size* likewise the vacuoles. The *latter* occurring in the light cells were of similar appearance to those which some-



Fig. 32. Part of taste bud from animal sacrificed 4 days after transection of the glossopharyngeal nerve. As in fig. 29 the cytoplasm contains products of degeneration but here they have clumped and formed inhomogeneous structures (arrow). Electron microscopy 17,600 x.

the number of cells, both light and dark, be reduced but also that they diminished in size (Fig. 30 and 31). The remaining light cells were populated by osmiophilic granules and also vacuoles. The nucleus had shrunk and was often pressed like a half moon against the cell membrane by the large osmiophilic clumps (Fig. 32). The cell limits cannot be followed and it was difficult to differentiate light from dark cells. The most obvious feature concerning the dark cells was that the osmiophilic particles were not of the same size and the vacuoles were considerably smaller. In the



Fig. 30. Taste buds from an animal sacrified 4 days after transection of the glossopharyngeal nerve. The reduction of the number of cells has started and the osmiophilic granules are clumped. The vacuoles appear especially around the light cell's nuclei. Phase contrast microscopy. 830 x

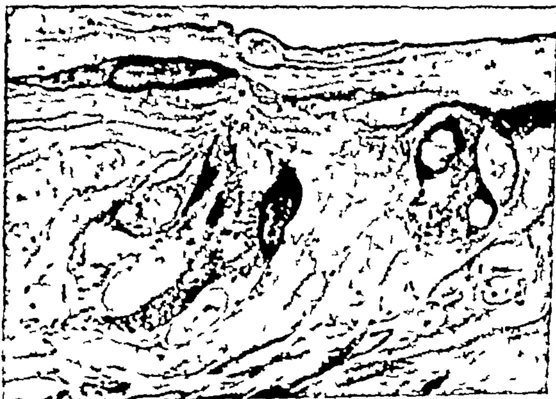


Fig. 31. Taste bud from an animal sacrified 4 da fter tran ection of the glossopharyngeal nerve. This figure shows differently t ined cell and the richness of granules in the cells. NZ staining (Maillet modified zinc iodin method). Light microscopy. 1,30



Fig. 32. Part of taste bud from an animal sacrificed 4 days after transection of the glossopharyngeal nerve. As in fig. 29 the cytoplasm contains products of degeneration but here they ha clumped and formed inhomogeneous structures (arrow). Electron microscopy 17,500 x.

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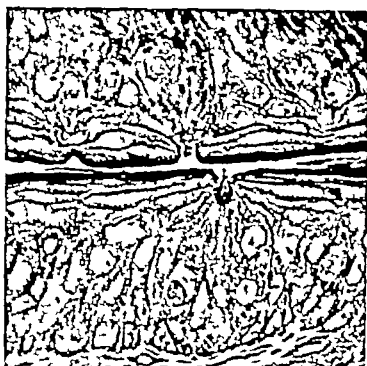


Fig 30. Taste buds from an animal sacrified 4 days after transection of the glossopharyngeal nerve The reduction of the number of cells has started and the osmiophilic granules are clumped The vacuoles appear especially around the light cell s nuclei. Phase contrast microscopy 830 x

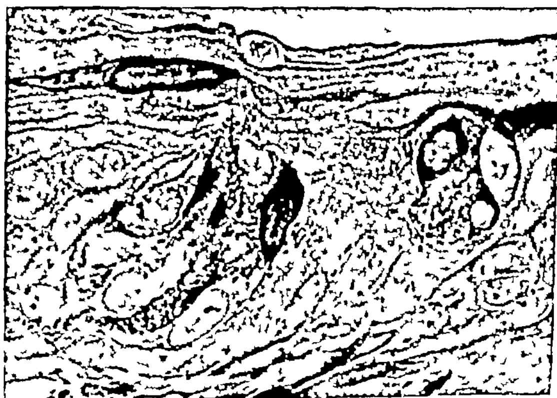


Fig 31 Taste bud from an animal sacrified 4 days after transection of the glossopharyngeal nerve This figure shows differently stained cells and the richness of granules in the cells. NZ staining Maillet modified zinc iodin method Light microscopy 1250



Fig. 34. Taste buds from an animal sacrificed 5 days after transection of the glossopharyngeal nerve. The left taste bud is more slender than the normal one. The taste pit is still intact. Intragemmally there occur osmiophilic granules of varying size. The membranes of the cells and nuclei are partly disappeared. Phase contrast microscopy 680 x.

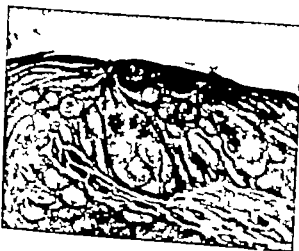


Fig. 35. Taste bud from an animal sacrificed 6 days after transection of the glossopharyngeal nerve. The taste bud is in a stage of degeneration and there are few cells left. Phase contrast microscopy 700 x.



Fig 33 Degeneration products in a light cell from a taste bud 5 days after transection of the glossopharyngeal nerve The osmiophilic clump has in some parts a filamentous whirl like structure and in others a more homogeneous appearance Electron microscopy 72.000 x

dark cells as in the light ones a considerable reduction of the cytoplasm had occurred as well a pyknotic degeneration of the nucleus The chromatin clustered in the peripheral region most often (Fig 33)

The degeneration which took place after nerve transection was, as pointed out earlier progressive From *the 5th to the 6th day* an obvious reduction in the number of taste buds occurred and the remainder diminished considerably in size The remaining cells were in a state of degeneration of the same appearance as described after the fourth to fifth day (Fig 34 and 35)

After *the 7th to the 8th day* however there were no taste bud like structures in the epithelium on the papillae. There were a few remnants of irregular osmiophilic clumps, vacuoles and some single cells noted on the



Fig 38. Taste bud from animal sacrificed 8 days after transection of the glossopharyngeal nerve. The remainder of a taste bud is only some single cells, vacuoles and granules. Phase contrast microscopy 1100 x.

Fig 39 Central part of foliate papilla with ridges and furrows from an animal sacrificed 14 days after transection of the glossopharyngeal nerve. No taste bud can be seen and the epithelium along the furrows is uninterrupted and stratified. Phase contrast microscopy 100



Fig 36



Fig 37

Taste bud from an animal sacrificed days after transection of the glossopharyngeal nerve In both these figures there are only some irregular cells left. Phase contrast microscopy Fig 36 630 x fig 37 70 x

site of the taste buds The taste pore was defective and the epithelium in the pores assumed a more and more regular stratification (Fig 36 and 37)

Between *the 8th and 14th day* after the transection of the glossopharyngeal nerve it was possible to find only a few remainders of degenerated products of taste buds in the epithelium (Fig 38)

The foliate papillae on rabbits which survived more than 14 days after the transection had a total loss of taste buds. The epithelium on the ridges was regularly stratified and without defects (Fig 39) The even cupola shaped top of the ridges had except in 2 rabbits been preserved. These 2 animals had a survival time of 30 and 90 days. The most superficial part of the epithelial layers seemed to disappear in these cases. For the rest



Fig. 38. Taste bud from an animal sacrificed 8 days after transection of the glosso-pharyngeal nerve. The remainder of a taste bud is only some single cells, vacuoles and granules. Phase contrast microscopy 1100 x.

Fig. 39. Central part of foliate papilla with ridges and furrows from an animal sacrificed 11 days after transection of the glossopharyngeal nerve. No taste bud can be seen and the epithelium along the furrows is uninterrupted and stratified. Phase contrast microscopy 100 x.



Fig 40



Fig 41

Cro s and longitudinally sec tioned nerves in th core of a f llate papilla from an animal sacrificed 3 days after transec tion of the glossopharyngeal nerve. The myelin sheaths are in different stages of degene ration nd the myelin is clum ped The a ons are still pre sent Phase contrast micro-scopy Fig 40 730 x fig 41 610 x

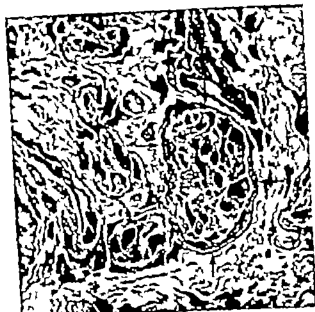


Fig. 42. Cross-sectioned nerve (arrows) in the subepithelial region in a foliate papilla from an animal sacrificed 6 months after transection of the glossopharyngeal nerve. No myelin can be seen but the presence of connective tissue is remarkable. Phase contrast microscopy 600 x.

the normal form of the foliate papillae was preserved. The furrows, however became shallower when the animals survived longer and the epithelium against the furrows had also thinned out.

The nerve structures situated subepithelially also passed through a degeneration process after transection of the glossopharyngeal nerve. This process was visible after 1 to 2 days. The normal myelin pattern disappeared. The round dark rings of myelin around the axon took on an ellipsoid shape, and became irregular or clumped together. In nerves longitudinally sectioned this clumping of the myelin was more easily observed. The myelin diminished after a certain time passed following nerve transection (Fig. 40 and 41). After 4 to 5 days it was possible to see only some myelin clumps in both longitudinally and cross sectioned specimens. The unmyelinated nerve fibers also took on a diffuse appearance. 10 to 14 days after nerve transection the myelin had disappeared. The outer structure of the nerves appeared but it was impossible to distinguish the individual fibers. The nerves were filled with connective tissue (Fig. 42). This picture appeared in all the specimens where the animal had survived for more than 30 days.

c. The structure after nerve suture

In this section of the investigation 19 rabbits have been used The time of survival and the number in each group is shown in table 6.

Table 6 *The number of rabbits and their survival time after suture of the glossopharyngeal nerve*

Survival time in days	10	14	30	90	180	210	240	270
Number	3	2	1	1	3	4	5	1

Macroscopic findings
The region with the foliate papillae on the rabbit's tongue was inspected via the operation microscope and the operated and unoperated side were compared The normal surface structure was preserved The furrows, however seemed to be shallower on the operated than on the unoperated side in animals killed more than 30 days after suture of the glossopharyngeal nerve. The papillae on these rabbits were paler on the operated than on the unoperated side

Microscopic findings
In rabbits which are killed *10 days* after suture of the glossopharyngeal nerve the foliate papillae have no taste buds of normal appearance There is a reduction in the total amount of taste buds and the remaining ones are in a degenerative stage and have the same appearance as those described in the chapter on nerve transection The subepithelial nerve structures have been changed and the regularity in the pattern of the myelinated nerves is lost The myelin remains only as solitary irregularly shaped clumps

14 days after suture of the glossopharyngeal nerve the papillae are completely devoid of taste buds and the epithelium present is regularly formed Myelinated nerves are also completely absent in the subepithelial tissue *1 3 and 6 months* after the suture there are still no taste bud like structures visible on the foliate papillae. As after only nerve transection the ridges and furrows are well preserved The furrows are however considerably shallower here than on the papillae of normal animals

The animals whose foliate papillae are examined *between 7 and 9 months* after suture of the glossopharyngeal nerve show indications of activity within the epithelium the regular pattern is disturbed The subepithelial tissue projects in the epithelial layer on the lateral side of the ridges. These projections of stroma are composed of besides connective tissue and nerve structures, also cell collections which in the beginning are arranged in irregular formations (Fig 43) These collections of cells are considered to be presumptive taste buds.



Fig. 43



Fig. 44.

Beginning of regeneration of the taste buds in f llate papillæ between 6 and 7 months fter suture of the glossopharyngeal nerve in both these figures Phase contrast microscopy Fig. 43 950 ; fig. 44 1100 x.

The presumptive taste buds are connected to the subepithelial tissue by a basement membrane and superficially by squamous cells. No taste pore can be seen. The cells inside the presumptive taste buds are elongated, and contain a nucleus. In the beginning the structures are not differently tained. With increased passage of time after the suture of the nerve, more cells in the epithelial layer take the shape of a taste bud-like structure (Fig 44) The epithelial surface is at last pierced and structures of definite

c. The structure after nerve suture

In this section of the investigation 19 rabbits have been used. The time of survival and the number in each group is shown in table 6.

Table 6 The number of rabbits and their survival time after suture of the glossopharyngeal nerve

Survival time in days	10	14	30	90	180	210	240	270
Number	2	2	1	1	3	4	5	1

Macroscopic findings
The region with the foliate papillae on the rabbit's tongue was inspected via the operation microscope and the operated and unoperated side were compared The normal surface structure was preserved The furrows, however *seemed to be shallower on the operated than on the unoperated* side in animals killed more than 30 days after suture of the glossopharyngeal nerve. The papillae on these rabbits were paler on the operated than on the unoperated side.

Microscopic findings
In rabbits which are killed *10 days* after suture of the glossopharyngeal nerve the foliate papillae have no taste buds of normal appearance There is a reduction in the total amount of taste buds and the remaining ones are in a degenerative stage and have the same appearance as those described in the chapter on nerve transection The subepithelial nerve structures have been changed and the regularity in the pattern of the myelinated nerves is lost The myelin remains only as solitary irregularly shaped clumps

14 days after suture of the glossopharyngeal nerve *the papillae are* completely devoid of taste buds and the epithelium present is regularly formed Myelinated nerves are also completely absent in the subepithelial tissue *1 3 and 6 months* after the suture there are still no taste bud like structures visible on the foliate papillae. As after only nerve transection the ridges and furrows are well preserved. The furrows are however considerably shallower here than on the papillae of normal animals.

The animals whose foliate papillae are examined between *7 and 9 months* after suture of the glossopharyngeal nerve show indications of activity within the epithelium the regular pattern is disturbed The subepithelial tissue projects in the epithelial layer on the lateral side of the ridges. These projections of stroma are composed of besides connective tissue and nerve structures, also cell collections which in the beginning are arranged in irregular formations (Fig 43) These collections of cells are considered to be presumptive taste buds.



Fig. 46.

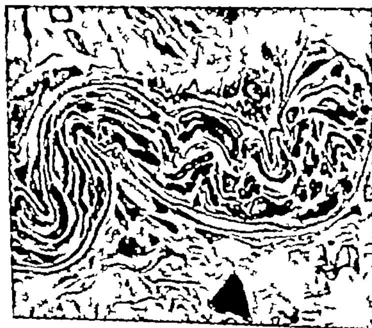


Fig. 47

Cross- and longitudinally sectioned nerves in the core of f[illegible] [illegible] papilla from [illegible] animal sacrificed 8 months after suture of the glossopharyngeal nerve showing regeneration of myelinated nerve structures. Phase contrast microscopy Fig. 46 [illegible] fig. 47 800 x.



Fig 45 Regenerating taste buds from a foliate papilla 8 months after suture of the glossopharyngeal nerve A taste pit is developed and is wider than a normal one Phase contrast microscopy 1160 x.

taste bud appearance are present. With the break through on the surface of the epithelium the pore has been formed The pores are wide and clumpy and most often there are several within the same taste bud Microvilli are at first not seen as a rule but in some pores they are seen at the apical ends of the taste bud cells The cells seem to reach from the basement membrane to the pore The nuclei are elongated and more darkly stained than the cytoplasm and situated in the lower two thirds of the cell (Fig 45)

Parallel with this development of taste bud like structures the myelinated nerves begin to regenerate. The myelin in the nerves however is not so regular and densely arranged as normally but occurs in irregular formations in the nerve bundles (Fig 46 and 47)

This development of taste bud like structures does not occur uniformly in the whole papilla In certain areas there is a total loss of taste buds of nearly normal appearance. Rabbits with a survival time of over 9 months after nerve suture have fully developed taste buds. The numbers vary however within the ridges some ridges completely lack a trace of taste buds

In all cases where suture of the glossopharyngeal nerve is carried out the nerve has been dissected out and the site of the suture examined when the rabbits are killed It is thereby established that in all cases the 2 ends of the sectioned nerve have grown together to form a new nerve.

microscopy Murray and Murray (1967) and Farbman (1965 a) show that those cells they describe as supporting cells are furnished with microvilli in their apical region also. These cells always reach up to the taste pit.

In the present investigation it is shown that all cells within the taste buds, reach to the taste pit and there they end in microvilli of varying length and number. Villi belonging to the dark cells appear to be more highly differentiated and of larger dimensions than those of the other cells. The occurrence of microvilli causes the cells to have a considerably larger contact surface in the pore. This without doubt, is of functional importance. If the microvilli also are furnished with fine macro-molecular surface differentiations this would increase the contact surface still further. But as pointed out earlier it is not possible to decide whether or not these structures occur on the most differentiated villi. The possibility of an artifact through a shrinking process in the preparation and fixing can not be excluded. Fawcett (1965) describes similar structures on the intestinal epithelium and says that they form a part of the cell membrane and take part in the resorptive process of the cell membrane in the intestine. Theoretically it can be the same in the taste buds.

There is no certain information concerning the significance which the various cytoplasmic organelles in the taste cells have from a functional viewpoint. The osmiophilic granules, which are of the same appearance as the osmiophilic substance in the taste pore, have as a rule been observed in the dark cells (Iriki, 1960, de Lorenzo, 1958, 1963 a, Nemetschek-Gansler and Ferner 1964, Farbman 1965 a, Murray and Murray 1967) but also appear in the light cells. They are however considerably smaller and not so numerous in the light cells (de Lorenzo, 1958, 1963 a, Iriki, 1960). The granules, which most frequently occur in the border zone against the taste pit, have been considered to be a sign that the cells possess a gustatory function and should thus be the result of a resorptive process. Murray and Murray (1967) put forward the view that granules are produced in the dark cells and the basic substance in the taste pore is a product thereof.

Osmiophilic granules, as shown in this study, are found in the dark cells and chiefly in the supranuclear portion of the cytoplasm just under the taste pit. The light cells also contain these granules, but as a rule, they are of considerably greater dimensions.

Iriki (1960) and de Lorenzo (1958, 1960, 1963 a) are the only electron microscopists, who have observed vacuoles in both cell forms. The author also has found vacuoles in both cell types.

Kolmer (1910) describes fibrillary structures in certain cells and considers this to denote a supporting function in the cell. In earlier electron microscopic studies (Trujillo-Cenóz, 1957, Farbman, 1965 a, Murray and Murray 1967) as in the present investigation, besides these fibrillary structures, also tubuli and others of microfilamentous character have been observed. In the author's investigation, many of the tubular structures have

IV DISCUSSION AND CONCLUSIONS

a The normal structure

The structure of the taste buds has as appears from the literature review been the object of extensive light microscopic studies. During the last decade electron microscopy has also been applied Even in the earliest studies on the structure of the taste buds it is possible to distinguish different types of cells This distinction is based mainly on the position within the taste buds the form size and the relationship to the nervous components.

There is unanimous agreement that the taste buds contain sensory cells. The occurence of supporting cells, on the other hand has been argued The majority of authors consider as appears from the literature review that this cell form does exist

It is pointed out in the description of the structure of the taste buds that there are small structural differences between the taste bud cells This is the reason why there are difficulties in classifying the cells. The majority of earlier authors divide the cells according to their function i e. into sensory cells and supporting cells in spite of the lack of physiological documentation

The author considers as more adequate to apply a descriptive division based on the general appearance of the nucleus and cytoplasm of the cells occuring in the rabbits taste buds. The main types of cells in both light microscopy and electron microscopy have been designated as light and dark cells Several authors have previously divided the cells from the same point of view but at the same time classified them from a physiological viewpoint The dark cells, as a rule have been regarded as sensory cells and the light ones as supporting cells (de Lorenzo 1958 1960 1963 a Iriki 1960 Nemetschek-Cansler and Ferner 1964) In the Murray group there is a certain doubtfulness about the division In 1961 both the light and the dark cells were regarded as gustatory but in 1967 the light ones were considered to be sensory cells Farbman (1965 a) has described 4 cell types where type I corresponds to the dark and type II to the light cells Murray and Murray (1967) like the author have not found any cell corresponding to Farbman s cells designated as peripheral and basal In all probability the peripheral cells are the counterpart to the perigemmal cells

The taste buds have a specific function and the cells have an ultrastructure different from that of the surrounding cells The taste pore is the only region where the taste bud stands in contact with the surface of the tongue through microvilli The taste pit contains an osmiophilic substance which is considered to be of importance for the stimulation of taste The earlier idea was that only sensory cells have contact with the pores. With electron

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a pronounced curved form It should be pointed out that microfilaments also occur in the infranuclear part of the both cell types

From the discussion it is evident that there are differences of opinion regarding the structure of the taste buds and the interpretation of the findings An explanation of this can be that various animals have been investigated namely monkeys (Murray and Murray 1960) rats (Gray and Watkins, 1965 Farbman 1965 a) and rabbits (Engström and Rytzner 1956 a b Trujillo-Cenóz, 1957 de Lorenzo, 1958 1960 1963 a Iriki, 1960 Nemetschek-Gansler and Ferner 1964 Murray and Murray 1967) But perhaps as pointed out by many authors, it might be that fixation is highly variable in quality In addition there are great individual variations in the taste buds in the same animal species.

The cells in this study designated light and dark have greater similarities than differences in structure. Both types of cells are furnished with microvilli of similar inner structure The relation to nervous components is the same and the greater part of the cytoplasmic organelles are of the same pattern. That which chiefly differentiates the cells is the varying density of the chromatin in the nuclei the formation of the endoplasmic reticulum and the distribution of osmiophilic particles. The cells which are designated otherwise have, as is clear from the earlier account, pronounced similarities with one or the other of the principal forms

Through experimental investigations (Beidler et al 1960 Beidler 1961 1963 Beidler and Smallman 1965 de Lorenzo, 1963 b Robbins, 1967) it has been proved that a continuous degeneration and renewal of cells occurs in the taste buds. In the perigemmal epithelial layer a continuous cell division takes place and the newly formed cells invade the center of the *taste buds, where after a time they degenerate*

Murray and Murray (1967) state "It might be argued that only one cell type exists since there seems to be a pattern of continuous transition from perigemmal cell through various stages to cell degeneration "

In the present work mitoses have not been seen and it has not been possible to decide if perigemmal cells are transformed to gemmal and there pass through various stages The fact that the cells in the taste buds do not show such great structural differences can be an indication that there is one cell form only which passes through various stages of development It seems as if the cell degeneration and cell breakdown especially affects the light cell form This can indicate that this cell is either a late stage in the further development of the dark cell and represents an aging form or that it represents a separate and more vulnerable cell

As a summary it can be pointed out that on the basis of observations made of the structure of the cells in the taste buds of the rabbit in spite of structural differences it cannot be definitely decided whether both sensory cells and supporting cells occur It is most probable however that the cells during their life-cycle pass through different stages. The results

of this study are mainly in favor of the view that in taste buds there is only one cell form which may have a different appearance and this cell must have a gustatory function

The nerves

Sometimes it is difficult to differentiate nerve structures from sensory cells, especially in the upper regions of the taste buds. The intragemmal nerves divide repeatedly in their course and end in a club-like, enlarged nerve ending. In earlier studies on warm-blooded animals it has not been possible to decide whether both afferent and efferent nerve endings exist. De Lorenzo (1963 a) has discussed this question chiefly against the background of showing different calibers in the nerve fibers and he has separated both the inner structure and various ways of contact with the receptors.

Desgranges (1966) in his studies of the taste buds on Ameiurus, an amphibian found nerves and nerve endings which are designated as afferent and efferent. These nerve structures, as is clear from the present investigation, appear richly in the basal region of the taste buds. Typical nerve endings are few but it is possible to distinguish 2 forms. One form is only sparsely furnished with vesicles and granules while the other is more richly supplied with these structures. In comparison with nerve endings in other sensory organs such as the cochlea and vestibularis, the former which is most commonly occuring, corresponds to afferent and the latter to efferent nerve endings. Both types of nerve endings stand in synaptic contact with either light or dark cells. Gray and Watkins (1965) have primarily studied the synaptic regions in the taste buds and they point out that these are not wholly typical or of the same appearance as those in other sense organs. Synapses with both vesicles and granules have been observed in the present investigation, but they are extremely sparse and this constitutes a phenomenon difficult to explain. In other sense organs and in regions with synaptic contact the synaptic regions usually appear distinct. For many years, at the same laboratory great interest has been devoted to the study of synapses between sensory cells and nerves. There has also been great interest devoted to the study of synapses in the central nervous system with exactly the same method as in e.g. the inner ear or medulla oblongata studies, where characteristic synaptic regions appear in great numbers (Engström, 1969)

Synapses should be found between receptor cells and nerve endings, but Farbman (1965 a) and Murray and Murray (1967) however have found synaptic contacts also in cells which they regard as supporting cells. In the present study synapses have been observed between all cell types and nerve endings. This observation can support the assumption that the intragemmal cells constitute one cell form in various stages of development and all with gustatory function.

This study confirms the statement of Gray and Watkins (1965) that

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The changes are best seen in the peripherally situated cells on the taste buds but they successively progress to the central portion. Parallelly there follows a structural degeneration also in the nerves running subepithelially

The foliate papillae from rabbits which are examined 1 3 6 and 9 months after nerve transection show a total loss of taste buds. Our studies have never indicated that extensive spontaneous degeneration of the taste buds happens with intact nerve function.

Von Vintschgau (1880) and Meyer (1896) consider that the disappearance of the taste buds after transection of the corresponding nerve takes place through de-differentiation or metamorphic transformation of the supporting cells in the taste buds but, not the sensory cells. Ranvier (1888) Olmsted (1921) Whiteside (1927) and Guth (1957) are of the opinion that a degenerative process takes place. In earlier works there are, however no detailed histological investigations of the course of events, when taste buds disappear after nerve transection. Robbins (1967) also discussed the possibility of inhibition of the mitotic activity and that the differentiation to mature cells is stopped. The above mentioned factors, plus the possibility of local circulatory disturbances and sensitivity disturbances with increased erosion of the mucous membrane will be discussed

Investigations (Beidler et al., 1960 Beidler 1961 1963 de Lorenzo, 1963 b Beidler and Smallman, 1965 Robbins, 1967) have shown that there is high mitotic activity in the perigemmal cells and that the newly formed cells wander into the center of the taste buds. In addition there is a *constant* breaking down of older cells taking place in the taste buds. The number of the intragemmal cells and the shape of the taste buds under normal conditions is unchanged. This is apart from the physiological age involution of the sense organ.

Robbins (1967) points out that the mitotic activity ceases after nerve transection. From this study it is evident that a rapid reduction of the number of cells in the taste buds occurs. This should indicate a decrease or reduction in the mitotic activity with reduced new cell formation Another possibility is that the nerve transection causes an increased cell breakdown. Under these conditions, however the total disappearance of the taste buds should not have occurred. It is most probable therefore that the mitotic activity does *not* go on in the normal way With diminished or wholly inhibited mitotic activity there will be no addition of cells in the taste buds and accordingly no differentiation.

The cells in the taste buds are highly collected in the bulb during the time of the process, even if at times it looks as they project into the surrounding tissue Artifacts, through incorrect sectioning cannot be completely excluded. This collection of the cells in groups discourages the idea of a de-differentiation or metamorphic transformation of the cells during the process.

In this investigation there has not been any study of the circulation in

synaptic contacts only exist between the receptor cells and the terminal dilatation of the axons

Kolmer (1927) like the author has observed ganglion cells in the subepithelial tissue The possibility that these ganglion cells belong to the glands in the subepithelial tissue cannot however be excluded

NZ staining

According to Maillet (1963) osmium tetroxid stains the structures which contain lipoproteins such as nerve endings and preganglionic and post ganglionic fibers in the autonomic system and motor end plates.

Through the staining of the taste buds it has not been possible to differentiate the nerve endings into afferent and efferent Besides nerve structures and cells the NZ staining of the taste buds has also brought to view a structure of special appearance which stretches from the nerve plexus under the taste bud to the pore The nature of this structure cannot be decided

b The structure after nerve transection

In most studies as appears from the literature review where taste nerves have been divided morphological changes in the taste buds are seen after some time These changes finally cause the total disappearance of the taste buds It is however not clear from the earlier investigations how the degeneration occurs in detail The process at least in warm blooded animals starts within 1 to 5 days after the nerve transection and is considered to be finished with total disappearance of the taste buds within 1 to 3 weeks.

Normally the taste buds of rabbits never have shown degenerative changes of an appearance and extent that have been observed after transection of the glossopharyngeal nerve. It can therefore be stated that the changes which occur in the taste buds after the transection are dependent on the broken nerve continuity

The process through which the taste buds degenerate and disappear starts within 24 hours after the nerve transection and is visible in both light phase contrast and electron microscope The process is progressive and after 14 days the taste buds have completely disappeared Both light and dark cells are affected by the changes The light cells get an increased vacuolizing within the beginning small vacuoles and these gradually increase and become confluent Osmiophilic granules and lysosomes are also formed in the cytoplasm The dark cells get an increase of osmiophilic granules and vacuoles appear in the cytoplasm Nuclear and cell limits are blotted out and finally there remains an unhomogeneous dark structure a product of degeneration which soon disappears A combined reduction in the size of the taste buds and the number of the cells within each taste bud occurs from the 4th day The changes are most easily followed in the light cells

c. The structure after nerve suture

The occurrence of taste buds in the studies of regeneration of gustatory nerves has been considered to be proof that a reinnervation has taken place.

From the review of the literature appears that suturing of a gustatory nerve after transection results in development of taste buds after some time. The circumstances are the same after the anastomosis of a central portion of a gustatory nerve with a non-gustatory. The results, however diverge when the central part of a non-gustatory nerve and the distal part of a gustatory nerve are sutured.

Earlier studies, as appears from literature review have shown that a degeneration of the taste buds takes place immediately after sectioning and suturing of gustatory nerves. After a varying interval of time taste bud-like formations are seen.

In the present study the glossopharyngeal nerve in rabbits has been sutured after transection. The foliate papillae are examined after various time intervals with regard to the occurrence of taste buds. As in only transection of the glossopharyngeal nerve, rabbits which are killed between 2 weeks and 6 months after suturing the nerve show a total lack of taste buds on the foliate papillae. 7 to 8 months after the operation the epithelium contains areas with structures which, in comparison with taste buds during development in fetal stage, show a remarkable resemblance (Farbman, 1965 b. Bradley and Stern, 1967).

It is possible to distinguish 2 steps in the course of events after suture of the glossopharyngeal nerve. In the first step the taste buds degenerate at the same time as changes occur in the nerves running subepithelially. In the second step the taste buds are reformed and the nerves regain their normal appearance.

In judging the results of this investigation there are a number of factors which can affect the course of events and therefore will be discussed in the following.

Circulatory disturbances. At the operation, the glossopharyngeal nerve is dissected free in the region where the division and suturing will take place. The operation is carried out with great care but injury to the fine capillary network with accompanying oedema in the nerve cannot be avoided. The nerve however is situated in soft tissues and has the possibility of expanding in its surroundings and will not be compressed. Serious disturbances to the function will not arise. Hence it is less likely that circulatory disturbances should influence the course of events and the result of the investigation. There would not have been total disappearance of taste buds either if there had been circulatory disturbances.

Innervation. Through anatomical studies (Chapt. B. I. a.) it is known that the taste buds on the foliate papillae on the rabbit's tongue are homolaterally innervated. The author's investigation concerning the taste buds after

the mucous membrane, either under normal or pathological conditions. In the examination no necrosis have been observed in the taste papillae except for in 1 case where there was a large necrotic ulcer Without doubt a profound transformation occurs in the taste buds after transection of the nerve but if a local circulatory disturbance contributes is not clear in that case. The histological picture would have been different and there would have been vast necrosis

In examination of the taste papillae there has been no indication of erosion of the surface epithelium except in the case just mentioned

All types of cells in the taste buds after nerve transection have changes of a morphological nature with degeneration products of lysosomal character in the cytoplasm and redistribution of the chromatin in the nucleus. Phagocyting cells are very seldom seen in the taste buds It is therefore less likely that the degeneration products are transported away through phagocytosis. Lysosomes normally contain a series of hydrolytic enzymes, which on the death of the cells are liberated and contribute to the dissolution of the cell (Norén 1968) Gahan (1965) has shown that the permeability of the lysosomes membrane is changed in connection with operative intervention on rat liver Hypothetically it can be assumed that changes in the permeability of the membrane of the lysosomes can also arise after nerve transection and this creates possibilities for the enzymes to affect the cytoplasm. Further studies can definitely solve this problem.

Olmsted (1920 a) May (1925) and Torrey (1934 1936) have in their studies on the effects of transection the taste nerves on cat fish discussed the possibility of a neurohumoral factor to maintain the connection between nerve and taste cell The process by which the taste buds in these cold blooded animals disappears, starts initially after some days with a free interval and ends within a few days The authors consider that the nerve normally contains this substance and that the amount in the peripheral stump would have been used up before the breakdown starts. Whiteside (1927) and Guth (1957) discuss this hypothesis and point out that the course of events in warm blooded animals is quite different from that in cold-blooded ones As pointed out above the degenerative process is of a progressive nature with immediate effect after the transection of the nerve Thus there is nothing that supports any agreement with the hypothesis of a neurohumoral factor

Summarizing, it can be pointed out that after transection of the glossopharyngeal nerve on rabbits structural changes arise in the taste buds cells on the foliate papillae. These degenerations finally lead to a total disappearance of taste cells These changes are in all probability the result of an inhibited mitotic activity and cell degeneration The fact that the cells within the taste buds vanish after nerve transection can be a support for the opinion stated in the summary of the normal structure *that in the taste buds there is only one cell type, which passes through various stages*

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Olmsted (1920 a) May (1925) and Torrey (1934 1936) have in their studies on the effects of transection the taste nerves on cat fish discussed the possibility of a neurohumoral factor to maintain the connection between nerve and taste cell The process by which the taste buds in these cold blooded animals disappears starts initially after some days with a free interval and ends within a few days The authors consider that the nerve *normally contains this substance and* that the amount in the peripheral stump would have been used up before the breakdown starts. Whiteside (1927) and Guth (1957) discuss this hypothesis and point out that the *course of events in warm-blooded animals is quite different from* that in cold blooded ones As pointed out above the degenerative process is *of a* progressive nature with immediate effect after the transection of the nerve *Thus there is nothing that supports any agreement with the hypothesis of* a neurohumoral factor

Summarizing it can be pointed out that after transection *of the* glossopharyngeal nerve on rabbits structural changes arise in the *taste buds cells on* the foliate papillae. These degenerations finally lead to a total disappearance of taste cells These changes are in all probability the result of an inhibited mitotic activity and cell degeneration *The fact that the cells within the* taste buds vanish after nerve transection can be a support for the opinion stated in the summary of the normal structure that in the taste buds there is only one cell type which passes through various stages.

C. CAN CHORDA TYMPANI BE REPAIRED?

From the present clinical study in Chapt. A IV it is evident that injuries to the chorda tympani with attending functional disturbances are far from unusual. This study only discusses these problems in connection with surgery for otosclerosis. However a large number of other operations are also performed in the middle ear either for hearing improvement or for cleaning. Temporal bone fractures sometimes cause damage to the chorda tympani.

From the experimental investigation in Chapt. B III. c. it is evident that a suture of the glossopharyngeal nerve in rabbits can give reinnervation and induce the development of taste buds on the foliate papillae. It is also supposed that the reinnervation is a direct result of the suturing of the nerve. The question arises Is it possible in man to suture the chorda tympani and get recovery of the loss of taste in that part of the tongue which is affected by the injury? So far as is known no such nerve sutures have as yet been carried out on the chorda tympani. In the following there will be a discussion of the various possibilities of restoring the continuity of the chorda tympani.

The chorda tympani can be accidentally of voluntarily injured with an interruption of the continuity in its course through the middle ear or in the bone in the posterior wall of the auditory canal. At radical mastoidectomy the nerve very often can be dissected free. The chorda tympani is under these conditions more easily accessible and it should be possible to restore the continuity The experiences from these operations can then be applied to other conditions It should be possible, although difficult, to restore the continuity of the chorda tympani when it is interrupted in the free course through the middle ear

Accidental interruption of the continuity of the chorda tympani can arise in the entrance of the nerve into the middle ear at the level of the posterior wall of the auditory canal. In certain cases it should be possible to dissect the proximal portion of the nerve free from the surrounding bone and get a little chorda-stump before it joins the facial nerve. Even in these cases it should be possible to restore the continuity of the chorda tympani.

However if the chorda tympani lesion is in the anterior portion of the

transection of the glossopharyngeal nerve unilaterally has shown a complete lack of taste buds ipsilaterally after 9 months Thus, there is no indication that the contralaterally coursing glossopharyngeal nerve should maintain or induce the formation of taste buds.

Spontaneous regeneration Through the nerve transection experiment partly here and partly in the studies of others it is shown that spontaneous development of the taste buds does not occur Nerve structures are seen to play an important role.

Relation nerve-receptor Embryological and experimental investigations on mammalia have shown that taste buds are dependent for their existence of intact nerve function Contrary to these are the experiments in urodele where tissue is transplanted from the tongue containing taste buds to the orbit, liver side-line organs or tail After a degenerative phase, regeneration of taste buds is proved (Stone, 1933 Mintz and Stone, 1934 Wright 1951 1955 1958) The authors consider that it is not possible for the transplanted tissue to have contact with gustatory nerves. The final conclusion is that taste buds can develop without the presence of nervous components. Poritsky and Singer (1963) showed however by means of nerve staining technique that there are regenerated nerve structures from orbital nerves in the transplanted tongue tissue when taste buds start to develop Special nerve staining has not been carried out in the above reported investigation. It is very likely that the authors had to revise their categorical conclusion if the nerve staining technique had been used

Robbins (1967) shows that after transection of the lingual nerve bilaterally but without suturing on a frog, reinnervation and development of taste buds arise through sprouting of fibers from the facial and glossopharyngeal nerves These experiments should support the idea that taste buds in cold blooded animals at least can develop without being induced by nerves carrying only gustatory nerve fibers The above discussed investigations of Boeke (1917) and Olmsted and Pinger (1936) can possibly also support the notion that the same conditions prevail in warm-blooded animals

Against the background of the results in this investigation and the unmistakable resemblance between those structures observed in this study after reinnervation and taste buds under development during the fetal period (Farbman 1965 b Bradley and Stern 1967) it must be supposed that a regeneration of taste buds has occured. Whether the regenerated taste buds possess functional properties cannot be decided on the basis of the present morphological study

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GENERAL DISCUSSION

Every year many patients go through different types of middle ear operations. The chorda tympani can then be lesioned accidentally or voluntarily. Temporary or permanent disturbances in the taste function of the anterior parts of the tongue may then arise.

As shown from the clinical part of this investigation patients with both preserved and divided chorda tympani at surgery for otosclerosis perceive taste impairments. In most earlier studies (table 1 and 2) the taste function has been recorded subjectively. As is pointed out in Chapt. A. V the patients sensation of taste impairment is influenced by several factors. The result of only subjective recordings must be valued critically. In this study the electrical taste test according to Krarup's electrogustometry and tests with solutions according to Börnstein have been used. These tests are objective but factors of subjective or psychophysical nature are included. Hence they cannot be considered as quite satisfactory. In practical work the methods, however, are applicable.

The chorda tympani contains taste fibers in the anterior two thirds of the tongue and dividing the nerve gives total loss of taste. No regeneration of the nerve after transection has been established. The chorda tympani has been divided in about 10 % during the surgery for otosclerosis. In comparison with earlier presented materials, the frequency is low (table 3). The course of the chorda tympani in the middle ear and its relation to the other structures reveals that it must be divided in some cases. The patients then perceive taste impairments. Even if the chorda tympani at the operation is preserved many patients experience permanent taste impairment.

This study *comprises* only the functional disturbances of taste after surgery for otosclerosis. The chorda tympani contains however, among other components, secretory fibers to salivary glands. Injuries to the nerve also can give disturbances in the salivary secretion (Wiberg, 1969).

The results in this investigation speak in favor of the opinion that the chorda tympani, whenever it is possible without jeopardizing the operation for otosclerosis, shall be preserved. Today bilateral stapes surgery is usual. This fact strengthens the opinion that the chorda tympani shall be preserved at the operation.

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middle ear the possibility of regaining the continuity is considered to be non-existent.

Special difficulties are afforded in the technical performance of nerve suture or other methods which will be discussed in the following In modern equipment for microsurgery of the ear there is a comprehensive instrumen tarium which can be adapted and used for the intended operation

By manufacturing extremely small fine needles it should be possible to restore the continuity in the chorda tympani with normal suture technique The suture material chosen must fulfil the highest demands of tissue compatibility not only regarding the nerve itself but also regarding the other structures in the middle ear

The *plasma clot method* (Tarlov et al 1943 Tarlov and Brooklyn 1944 Tarlov and Boernstein 1948) is conceivable for use in certain cases of adaptation of the divided nerve ends but the method has its limitations This has been pointed out by among others, Edshage (1964) in the following way "the junction however in practice proved to be so weak that the plasma clot had to be combined with epineurial suture Edshage (1964) too, has discussed the following methods for joining transected nerves Union of nerve ends by tubular splicing Epineurial sleeve and Venous sheath fat seal He has pointed out that these methods are often technically difficult to carry out and traumatic for the nerve. If these methods are not applicable on free running peripheral nerves, it is inconceivable to apply them to the nerve in question which besides being inaccessible is also very thin Finally the possibility of using clips" of resorbent or permanent material to join the nerve ends should be investigated

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In order to interpret the results, the normal structure of the taste bud must be known as well as the morphological changes after nerve transection.

Studies about the structure of the taste buds under normal conditions are extensive. The earliest investigations were performed by using light microscopy In the last decade however electron microscopy has been used The interpretation of the morphology in respect to various cell forms, the relation to nerve structures and the pattern of innervation are different

The foliate papillae on rabbits have been studied As is pointed out by others, difficulties in getting suitable and applicable fixing technique exist. Veronal buffered 1 5 % osmic acid solution and in some cases glutaraldehyde or Maillet s modified zinc iodine solution (NZ staining) have been used and it has been possible to analyze the structures in both light phase contrast and electron microscopy

Normally the taste buds contain cells which in various fixings and stainings appear differently This has resulted in various authors describing several cell forms As is seen from the discussion in Chapt. B IV a the most accepted opinion is that taste buds contain supporting and sensory cells. Difficulties exist in classifying the cells into different groups from a physiological point of view on the basis of structural differences. In view of the appearance of the cells they have been termed light and dark cells. Normally the cells in the taste buds have on their surface microvilli reaching into the taste pit. Generally the light cells contain villi not so well developed as that on the dark cells and the light cells seem to be older than the dark ones Both cell types contain osmiophilic granules and vacuoles The light cells however have numerous vacuoles and a few granules, while the dark cells have a few vacuoles and many granules The other organelles have the same appearance in both cells. Synaptic contacts have also been observed *between the nerve endings and both cell types. The nerve endings seem to be* afferent and efferent Some of the cells in the taste buds have an uncharacteristic appearance and cannot be assigned to the two main groups. It is impossible to state if they are intermediary forms

The findings in this investigation are in agreement with other results But earlier electron microscopic authors have always tried to classify the cells from a physiological aspect and then attempted to find out as many differences as possible in the cells.

It may be stated on the basis of the results in this investigation that it seems plausible that the cells have the same basic structure but *pass different* stages the light cell seems to be the oldest and the dark the youngest.

Earlier studies, when the taste nerves have been divided have shown that the taste buds degenerate and after some time disappear completely The course of events however has not been studied in detail

In this investigation the glossopharyngeal nerve has been excised on the rabbits just below the entrance and close to the base of the skull This nerve has been chosen because it is easy to reach As early as 1 to 2 days *after* transection of the nerve, the cells *in the taste buds* show degenerative changes The process proceeds and after 14 days there is a total loss of taste

buds. In the beginning, the vacuoles increase in size and number and the granules increase in both cell forms. The osmiophilic granules, especially in the dark cells increase in size. Some of the granules seem to be lysosomes. The number of cells is reduced and the size of the taste buds diminishes with time. As is pointed out in the discussion in Chapt B. IV b., changes which are observed in the taste buds after transection of the nerve are dependent upon a blocked mitotic activity and resulting in a degenerative process. The subepithelial coursing nerves also show degeneration.

Further confirmation that the cells in the taste buds normally pass through different stages during life span is shown after studying the structure of the taste buds after transection of the nerve. It can be established that all cells in the taste buds contain degenerative changes which with time lead to total disappearance of the taste buds. The fact that the same changes occur in all cells may support the interpretation that all cells have the same origin. The cells may be considered to be gustatory. The taste bud may be interpreted as a structure with specific function situated in the epithelium of the tongue papillae.

No spontaneous regeneration of the taste buds occurs after transection of the nerve which contains gustatory fibers in the corresponding region. Studies on the taste buds after partial denervation of the glossopharyngeal nerve have not been performed. The continuity of the nerve must be restored.

Only a few earlier studies exist where the taste nerves after transection have been sutured. The histological documentation, however, is defective. In the last part of the present investigation the glossopharyngeal nerve was sutured after the transection to restore the continuity. A degenerative process of the same type as seen after transecting only the nerve is seen. Also there is total disappearance of the taste buds occuring after about 2 weeks. No taste buds can be seen until about 6 to 7 months. 7 to 8 months after the suture of the nerve, at the foliate papillae, structures can be seen that form the presumptive taste buds. From a morphological point of view a great many taste buds of the same appearance as seen normally can be observed. The subepithelial coursing nerves also show regeneration with new formations of myelin. Whether these regenerated taste buds possess functional qualities cannot be decided by this study. Physiological studies in the future may solve these problems.

It can be stressed that suture of the glossopharyngeal nerve in rabbits gives a regeneration of the nerve which induces development of taste buds at the foliate papillae. This does not necessarily imply that suturing of the chorda tympani should result in regeneration of taste buds. The circumstances can be otherwise with respect to the chorda tympani as well as human beings. It can, however, as is pointed out in Part C, be a reason for restoring the continuity of the chorda tympani in a number of cases and with special instruments where it has been divided at middle ear surgery.

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Only a few earlier studies exist where the taste nerves *after transection* have been sutured. The histological documentation, however is defective. In the last part of the present investigation the glossopharyngeal nerve was sutured after the transection to restore the continuity A degenerative process of the same type as seen after transecting only the nerve is seen. Also there is total disappearance of the taste buds occuring after about 2 weeks. No taste buds can be seen until about 6 to 7 months. 7 to 8 months after the suture of the nerve at the foliate papillae structures can be seen that form the *presumptive taste buds*. From a morphological point of view a great many *taste buds of the same appearance* as seen normally can be observed. The subepithelial coursing nerves also show regeneration with new formations of myelin. Whether these regenerated taste buds possess functional qualities cannot be decided by this study Physiological studies in the future may solve these problems.

It can be stressed that suture of the glossopharyngeal nerve in rabbits gives regeneration of the nerve which induces development of taste buds at the foliate papillae. This does not *necessarily* imply that suturing of the chorda tympani should result in regeneration of taste buds. The circumstances can be otherwise with respect to the chorda tympani as well as human beings It can however as is pointed out in *Part C* be a reason for restoring the continuity of th chorda *tympani* in a number of cases and with special instruments where it has been divided at middle ear surgery

SUMMARY

The present investigation consists of three parts. The first part is a clinical study and gives an account of the taste function after surgery for otosclerosis. The second part is an experimental study and describes the structure of the taste buds on rabbits' foliate papillae under normal conditions, after transection of the glossopharyngeal nerve and after suture of the glossopharyngeal nerve. The third part comprises a discussion of methods to restore the continuity of the injuried chorda tympani in humans.

A survey of the literature on the course and function of the chorda tympani in human is presented as well as methods to examine the taste function in clinical practice. In tabular form are the investigations about the taste of patients operated upon for otosclerosis where the chorda tympani is divided or preserved. The frequency of divided chorda tympani at stapes surgery is also reported.

In 141 patients operated upon for otosclerosis the taste function was followed for 12 months or more. In 34 of the patients the chorda tympani was divided during operation. Subjective taste impairment was registered. *Objective taste tests were applied using electrical stimulation according to* Krarup and stimulation by solutions according to Börnstein.

If the chorda tympani was preserved 9 % of the patients had subjective *taste impairment more than 12 months after operation. The corresponding* number was 2 % when the chorda tympani was divided. The objective tests showed impairment in as much as 50 % of the patients if the chorda tympani was preserved and in 100 % if it was divided.

From the results it can be concluded that the chorda tympani whenever it is possible without jeopardizing the stapes operation shall be preserved. The conclusion is strengthened by the fact that the number of patients undergoing bilateral stapes surgery increases every year.

In the experimental section is a survey of the literature on the normal taste sensory organ, its development under the fetal period, the innervation, the occurence of papillae and taste buds and the structure from a macroscopic as well as a microscopic point of view. The structure of taste buds after transection and after suture of gustatory nerves is reviewed.

Taste buds from rabbits' foliate papillae have been studied in light, phase

contrast and electron microscope The results are presented and illustrated by several photomicrographs.

Normally the cells in the taste buds have in view of their appearance been termed light and dark cells. Some of the cells however have an uncharacteristic appearance and cannot be assigned to the main groups. Synaptic contacts have been observed between the nerve endings and both cell types. The cells seem to have the same basic structures and pass through different stages the light cell seems to be the oldest and the dark the youngest.

Transection of the glossopharyngeal nerve causes changes of a degenerative nature in all cells of the taste bud and finally total disappearance of the taste buds. This fact supports the interpretation that the cells have the same origin.

It thus can be stressed that in the taste buds of rabbits there is one cell form which passes different stages during life span. The cell may have a gustatory function. The taste bud may be interpreted as a structure with specific function situated in the epithelium of the tongue papillae.

No spontaneous regeneration of taste buds occurs after transection of the glossopharyngeal nerve Studies on the taste buds after partial denervation of the glossopharyngeal nerve have not been performed. Suture of this nerve in rabbits gives regeneration of the nerve The regenerated nerve induces development of structures which from a morphological point of view seem to be taste buds. It cannot be decided if these regenerated taste buds possess functional qualities.

In th last part of the present study there is a discussion of methods for restoring continuity of the injured chorda tympani. The experimental part shows that in rabbits regeneration of taste buds occurs after suture of the nerve belonging to the region. The circumstances can be otherwise in human beings. It may however in some patients be reason to try to restore the continuity of the *chorda tympani* when it has been divided at surgery for otosclerosis. In the future the methods will be elaborated

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Taste buds from rabbits foliate papillae have been studied in light phase

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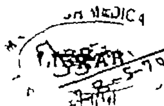
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SUPPLEMENTUM 258

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BILATERAL LESIONS OF THE TEMPORAL LOBE

A Case Study

JAMES JERGER, NORBERT J. WEIKERS, FRANK W. SHARBROUGH III, and SUSAN JERGER

UPPSALA 1969

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PREFACE

This monograph presents extensive data on a single patient We feel that the effort is justified by the extraordinary set of circumstances leading to the identification and evaluation of this unique hearing disorder

The patient was a 21 year-old member of the United States Air Force During an 8-month period from August 1967 to March 1968 he sustained two separate cerebral hemisphere infarctions the first on the left side the second on the right side Damage was maximal in the temporal lobes. The first episode produced no apparent deficit in auditory sensitivity but the second produced severe bilateral hearing loss. Thanks to the monitoring audiometry program of the Air Force both premorbid status and postmorbid changes in auditory sensitivity were well documented.

We feel that this patient s findings are unique for two reasons first because he demonstrated the reality of cortical deafness as a clinical entity and second, because he presented an unusual opportunity to study impairment of auditory function consequent on bilateral temporal lobe damage Through the cooperation of the United States Air Force we were able to gather extensive psychoacoustic data during a one-week period of intensive testing. The results are detailed in succeeding chapters.

This study would not have been possible without the generous assistance of Major James Endicott, USAF and Mr Alan Rost, of the Audiology Section, Wilford Hall USAF Hospital, who carried out all of the initial audiometry and successfully coordinated the subsequent audiologic evaluation. Their contribution is gratefully acknowledged We are indebted to Mr James Thelin for his valuable assistance in the collection and analysis of data, and t Mrs. J Ward Williams for the preparation of illustrative material.

I INTRODUCTION

The concept of cortical deafness has been the subject of some controversy considerable confusion but little information. Even the extent of the primary auditory cortex in the human has not been clearly defined. There is general agreement that the temporal lobes, and particularly the transverse temporal gyri, constitute at least a major portion of this functional unit, and that each cochlea is bilaterally represented (Crosby Humphrey and Lauer 1962) Indirect evidence obtained from animal experimentation implicates scattered regions of parietal and insular cortex as well (Pribram, Rosner and Rosenblith, 1954 Woolsey 1960) It is, therefore, not at all surprising that unilateral temporal lobe lesions do not lead to any gross auditory disorders either in animals or in man (Bunch, 1928 Mettler 1934 Penfield and Evans, 1934 Goldstein, Goodman, and King, 1956) Conventional audiometric tests, like the pure tone audiogram and routine speech discrimination tests, exhibit no significant abnormalities as the result of such lesions. Rather specialized testing techniques are required to demonstrate that such unilateral lesions indeed have any effect on auditory function. The defects most readily demonstrable are in impairment in the ability to localize sound in the contralateral auditory field (Sanchez-Longo, Forster and Auth, 1957) and a deterioration in the discrimination of distorted, interrupted or accelerated speech in the contralateral ear (Bocca, Calearo, Cassinari, and Migliavacca, 1955 Bocca, 1958 Jerger 1960 *b* Jerger 1964)

Conversely experimentally produced lesions of both temporal lobes in animals can produce marked diminution in hearing (Mettler 1934) In man, *bilateral* temporal lobe lesions are rarely produced surgically and, when produced are intentionally confined to the anterior portions, whenever possible thus sparing the transverse temporal gyri, as illustrated by the case described by Terzian and Dalle Ore (1955) In this patient, marked changes in behavior and in visual gnostic functions occurred, but no obvious auditory or aphasic disturbances were detected. Neither do auditory disturbances necessarily occur even in the face of rather marked bilateral posterior temporal lobe *disease* (Landau, Goldstein and Kleffner 1960) However frank hearing loss thought *to be due to cerebral disease* has been reported only in patients with demonstrable or presumed, naturally-occurring lesions in both *posterior temporal* lobes (Mott, 1907 Henschen, 1917 Bramwell, 1927 Misch, 1928 Clark and Russel, 1938 Lemoyne 1944 Lemoyne and Mahoudeau, 1959 Maspetiol, Messmiy and Semette 1959 Hansen and Rieske-Nielsen, 1963) Yet even these cases

II CASE HISTORY

First admission

The patient, a white male telephone maintenance worker was 20 years old when he was first admitted to the Wilford Hall USAF Hospital on 29 August 1967 He is left-eyed, right footed and ambidextrous, using his left hand for such tasks as writing and his right hand for eating and bowling. On the day of admission to the hospital, shortly after rising and eating breakfast he had experienced the abrupt onset of left frontal headache, numbness and paresthesias of the right hand and difficulty in the production and in the understanding of speech. He denied disturbance of consciousness, weakness, palpitations and other cardiac symptoms, recent illnesses, and the recent intake of medications.

There was no past history of rheumatic fever other cardiac disease thrombophlebitis and other thromboembolic diseases, migraine or significant head trauma. There was no family history of heart disease cerebrovascular disease migraine hypertension or diabetes mellitus.

The patient appeared inappropriately unconcerned and smiling. Height 69 inches. Weight 134 pounds. Pulse 100 per minute. Blood pressure 160/78 General physical examination was within normal limits Carotid pulses and peripheral pulses were full. There were no cervical or cranial bruits. Whispered voice Schwabach, Rinne and Weber tests revealed normal hearing. However he was thought to have a mild receptive phasia as evidenced by occasional inappropriate responses to questions and instructions. He spoke freely and spontaneously with frequent pauses, as if searching for words. He volunteered the information that he knew what he wanted to say but could not do so Paraphasia was also evident thus, he said knives" instead of needles" patches" instead of "matches" hander" instead of "handle and pea" instead of "pen Both spontaneous writing and writing from dictation exhibited word, syllable, and letter reversal and skipping. H read fluently within the limitations of his dysphasia, making no more errors than during conversational speech. There were questionable flattening of the right nasolabial fold, slight hypalgesia and hypesthesia distally in the right upper extremity and absence of abdominal reflexes on the right Neurological examination was otherwise entirely unremarkable

Hematocrit, hemoglobin, white blood cell count, sedimentation rate, urinalysis, blood urea nitrogen, serum creatinine fasting blood sugar serum cholesterol and electrocardiogram were within normal limits. X rays of the chest and skull were normal. Lumbar puncture revealed normal pressure

have not been universally accepted as being representative of cortical deafness. Thus, for example Goldstein denies the existence of even a single convincing case study in which there is an unequivocally measured reduction in (auditory) sensitivity with a clearly demonstrable CNS lesion and no demonstrable peripheral lesion" (Di Carlo Kendall and Goldstein 1962) Among the cited inadequacies of the published case studies are the following (1) existence of only anecdotal information concerning premorbid auditory function (i e., lack of premorbid audiometric studies) (2) *history of tinnitus and/or vertigo not usually expected with cortical disease*, or a failure to report their absence (3) advanced age of the patient raising the possibility of presbycusis, (4) failure to report a negative family history of deafness, (5) failure to report a negative history of excessive noise exposure (6) intake of ototoxic drugs or failure to report a negative history thereof (7) significant head trauma or failure to report a negative history thereof (8) presence of systemic desease that could affect eighth nerve function or inadequate data to exclude such a possibility (9) presentation of only behavioural audiometry and failure to report results of *electrophysiologic (i e electrodermal and/or electroencephalic)* audiometry and (10) lack of histopathologic studies of cochlea and auditory nerves at autopsy In each of the previously reported cases, many of these objections were pertinent

We have had the opportunity to study a young patient with deafness clearly due to cerebral disease Since he has survived his illness, histopathologic study of cochlea and auditory nerves was not available However all of the other objections have been answered by the data to be presented including premorbid audiometry For this reason and because of the *apparent rarity of this entity the case is presented in considerable detail*

exhibiting a moderately clear area of increased uptake in the left temporal region (Fig. 2 A and 2 B) EEG ten days after admission was normal A percutaneous left carotid arteriogram was done 13 days after admission This exhibited nonfilling of the angular and posterior parietal branches of the left middle cerebral artery during the arterial phase and retrograde filling of these branches during the late capillary and early venous phases (Fig. 3 A and 3 B)

The patient s production and understanding of speech and his hand writing improved gradually Two months after admission the following tests were administered Wechsler Adult Intelligence Scale Bender-Gestalt, Wechsler Memory Scale Form II Minnesota Percepto-Diagnostic Test, Kahn Test of Symbol Arrangement and the Eisenson Test for Aphasia The patient still had some discrete mild to moderate expressive and receptive aphasia. He could count, write numbers and letters, spell correctly from dictation, name objects and do arithmetic computations The only expressive ability involved was oral reading. In this area he exhibited sound substitution, such as rub" for run" and fable" for "table" It was also noted that many questions had to be repeated before the patient would respond some distractibility and a somewhat frenzied, disorganized approach in solving visual-motor tasks were noted. Overall, however there had not been severe deterioration Intellectual functioning was in the aver age range with a verbal IQ score of 97 performance IQ 98, and *full scale* IQ 97 The patient himself felt that he had returned completely to normal. He was discharged from the hospital two months after admission an l was able to return to his usual duties. There had been no subjective complaint o objective evidence of hearing loss throughout the period of observation. No audiometric studies were accomplished during this admission.

Second admission

The patient was readmitted to the hospital on 20 March 1968. In January 1968 he had begun noting increased nervousness and excessive sweating. Otherwise he had felt well until the day of admission. W eight loss and heat intolerance were denied.

He had retired on the night prior to admission, feeling and hearing well, and had set his alarm clock as was his custom When he awoke the fol lowing morning, h found his alarm clock had rung 30 minutes previously and had failed to waken him He was also immediately aware that the world about him was *strangely silent* He could not hear the running of water from the f ucet, the buzz of his electric razor or the sound of traffic on the street When others spoke to him, he heard nothing and was able to comprehend what wa being said only with great difficulty by carefully observing their lips and gestures. He experienced no headaches, tinnitus, vertigo r other symptoms referable to the ears or to the central nervous system, and he denied excessive noise exposure, the intake of ototoxic drugs, a history of titis media or a family history of deafness.

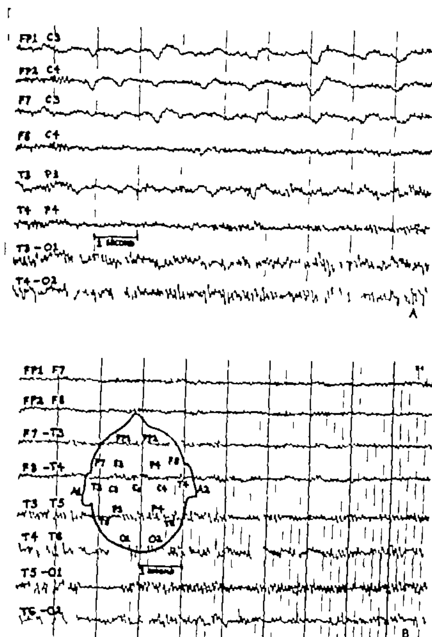


Fig 1 Electroencephalograms. (A) On d y of first dmis ion (29 August 1967) 25 minutes after st rti g hypery ntilati n, xhibiting delta activity over left nterior hemisph re (B) On day of second admissi n (20 M rch 1968) prior t utilizati n f ctivati n techniqu s, exhibiting theta activity over right posteri r h misph re

and clear CSF which contained no red or white blood cells, 60 mg percent sugar and 17 mg percent protein CSF VDRL was non reactive Resting EEG was normal during hyperventilation, rhythmical delta activity occurred in brief bursts over the left hemisphere only (Fig 1 A)

Pulse and blood pressure became normal within 24 hours and remained so thereafter The neurological abnormalities disappeared in three to four days. Technetium 99m brain scan one day after admission was abnormal





was normal. Except for being loud, his speech was normal. Weight 135 pounds. Pulse 110 per minute. Blood pressure 158/70. Pulses were again full to palpation, and there were again no cervical or cranial bruits. The skin was warm and moist. The thyroid gland was diffusely enlarged to an estimated twice normal size, the right lobe being larger than the left. He had slight lid lag, poor convergence and a fine tremor of the outstretched hands. Schwabach and Rinne tests confirmed the presence of marked bilateral sensori-neural hearing loss. General physical and neurological examinations revealed no other abnormalities.

Hematocrit, hemoglobin, white blood cell count, platelet count, sedimen

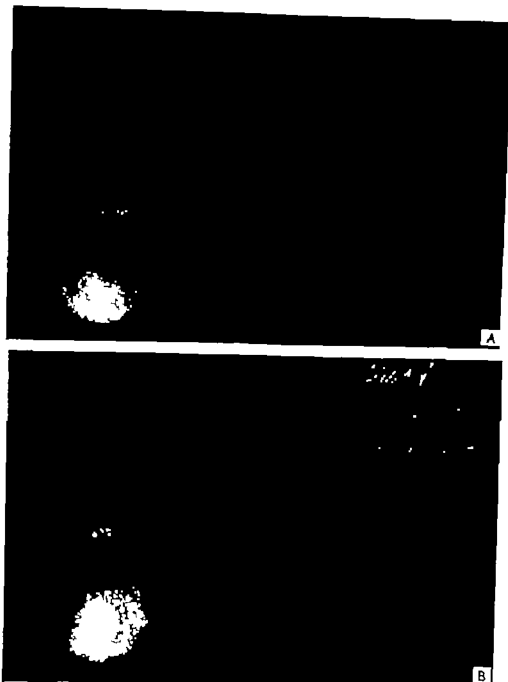
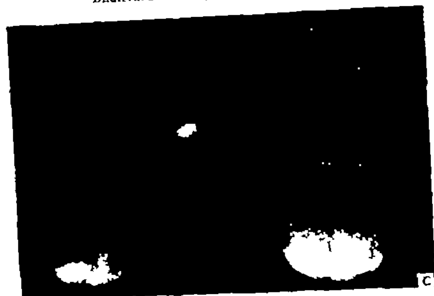


Fig. 2 Technetium ᵐ brain scintiphot graphs. Three phot graphs, at varying camera techniq s, are t ken in each projecti n. (A and B) Left and ight l t ral views, during first admissi n (30 August 1967) exhibiting moderat ly cl area f incre sed radioactivity in left temporal region. (C and D) Left and right l teral views, during second dmi ion (2 April 1968) exhibiting well-d fined re f incre sed radioacti ity i ight tempero-pariet l region and cleari g f th previ s left temporal abnormality

He again appeared inappropriately amused by his plight He exhibited no response to relatively loud noises Communication with him was established through writing, gestures and deliberate mouthing of words He responded appropriately to questions and instructions His hand writing





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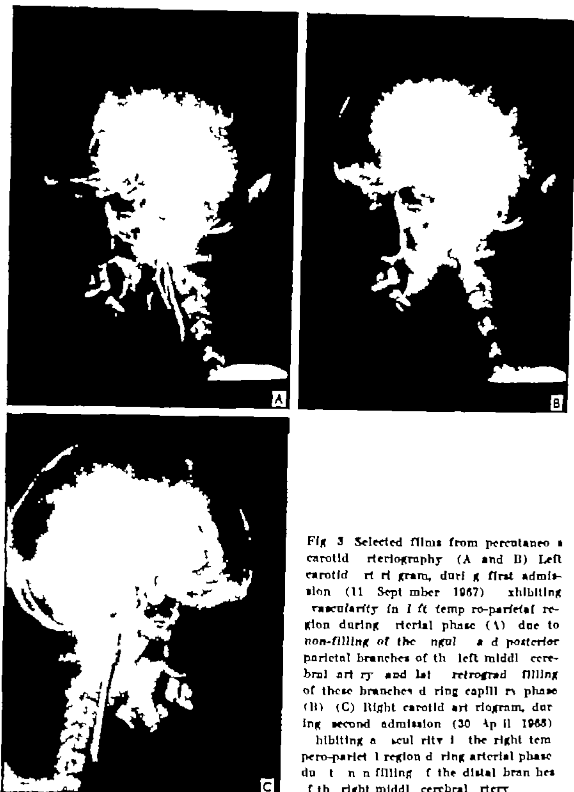


Fig 3 Selected films from percutaneo s carotid rteriography (A and B) Left carotid rt ri gram, duri g first admission (11 Sept mber 1967) xhibiting vascularity in l ft temp ro-parietal region during rterial phase (A) due to *non-filling of the ngul a d posterior* parietal branches of th left middl cerebral art ry and lat retrograd filling of these branches d ring capill ry phase (B) (C) Right carotid art riogram, dur ing second admission (30 Ap il 1968) hibiting a scul rity i the right tem pero-pariet l region d ring arterial phase du t n n filling f the distal bran hes f th right middl cerebral rtery

tation rate prothrombin time, partial thromboplastin time serum cholesterol fasting blood sugar 2 hour post prandial blood sugar serum electrolytes, serum calcium and phosphorus, blood urea nitrogen serum creatinine, serum bilirubin, serum alkaline phosphatase, bromsulfalein retention

and urinalysis were either negative or within normal limits. Blood VDRL nonreactive The LE phenomenon was not observed on four preparations of blood and on one supravital preparation of the buffy coat Latex globulin slide agglutination test was negative on three occasions. Serum protein electrophoresis revealed albumin 3 7 alpha-1-globulin 0.3 alpha-2-globulin 1 0, beta-globulin 1 1 and gamma-globulin 1.5 gm percent (normal 3 9–5.2, 0.2–0.35 0 4–0 7 0.56–0.83 and 0.6–1.5 gm percent respectively) Serum immunoelectrophoresis revealed gamma-G 1150, gamma-A 340 and gamma-M 98 mg percent (normal 1200 ± 226, 195 ± 91 and 116 ± 55 mg percent respectively) There was slightly increased rouleaux formation on peripheral blood smear Serum viscosity 1.99 relative to water (normal 1 4–1.8) The Sia test was negative Protein bound iodine 11.3 micrograms percent RAI uptake 44% at 24 hours (normal 10–30%) Thyroxine binding index 0 77 (equivalent to T³ resin uptake of 41.5%) Thyroid scan showed the thyroid gland to be twice normal size, the right lobe being the larger X rays of the chest and electrocardiogram were normal

Ice-water caloric tests produced normal symmetrical responses. Skull X-rays and tangent screen visual fields were normal. Ophthalmodynamometric retinal artery pressures were 70/20 mm Hg bilaterally Lumbar puncture revealed normal pressure and clear CSF which contained no white blood cells, 12 red blood cells per cu mm, 95 mg percent sugar and 14 mg percent protein. CSF VDRL was nonreactive. EEG on the day of admission was abnormal exhibiting occasional, rhythmical 3–4 Hz activity over the right temporal region (Fig. 1 B) Repeat EEG two months later was normal. Technetium-99m brain scan 13 days after admission was abnormal, demonstrating a prominent area of increased uptake in the right tempero-parietal convexity region (Fig. 2 C and 2 D) Repeat brain scan one month later was equivocally abnormal, demonstrating a faint area of increased uptake in the same area. A percutaneous right carotid arteriogram was done six weeks after admission. This exhibited non filling of the distal portions of the right middl cerebral artery with retrograde filling of these vessels during the capillary nd early venous ph ses (Fig. 3 C)

Ten weeks after admission, after partial recovery had occurred, Bender-Gestalt Sentence Completion Test and Wechsler Adult Intelligence Scale were administered Mild receptive and expressive aphasia were again detected O rall intellectual *functioning fell* within the normal range with a erbal IQ score of 87 performance IQ 103 and full scale IQ 93, representing declines of 10 and 4 points in the verbal and full scale scores and a poi t rise in the *performance* score compared to the previous testing. The Wechsler subtest scores, compared to those previously obtained, indicated a recovered ability to perform psycho-motor tasks and good visual-motor coordination but a *significant* deterioration in the Digit Span test. This latter combined with his good qualitative performance in the Bender-Gestalt test, was int rpreted as being a reflection of his auditory and aphasic problems rather than an indication of memory *impairment*.







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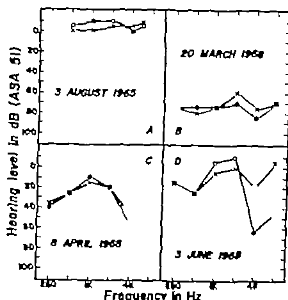


Fig 4 Pure tone air conduction audiograms. o o = Right ear x–x = l ft ear (ASA-51) (A) Pri r to onset of illness (3 August 1965) exhibiting normal hearing at ll freq encies in both ears. (B) O d y of second admission (20 March 1968) exhibiti g marked hearing l ss at all frequencies bil terally (C nd D) During recovery phase second dmissi n (8 April 1968 and 3 J n 1968) exhibiting in both e rs return t w rd normal, especially at speech frequencies, with persistent marked loss at high frequencies in right ear

Continuous gradual improvement in hearing, the details of which are presented below occurred during hospitalization His resting pulse remained elevated pulse pressure remained wide and he continued to appear clinically hyperthyroid A single dose of 10 millicuries I[131] was administered orally and several weeks later reserpine 0 25 mg daily was added

Tests of language function

Language function (10 weeks after admission, after considerable pure tone sensitivity had returned as demonstrated below)

Articulation was normal Occasional paraphasic errors persisted during spontaneous speech with repetition and on reading aloud Grammar sentence form and phrasing, cadence of speech, speech rhythm and vocabulary were normal The patient was requested to repeat words pronounced by the examiner first with his eyes open and observing the examiner then with his eyes covered Very few errors occurred when the patient had his eyes open Occasional errors occurred when the patient had his eyes covered and the examiner stood to the left of the patient With eyes covered and examiner to his right the patient was able to repeat very few words accurately He read accurately both quietly and aloud within the limits of his dysphasia, and he exhibited good reading comprehension He exhibited

no abnormalities in writing spontaneously from dictation and by copying. He made no spelling errors. With eyes closed, he was able to identify the sounds of running water and a telephone ringing, but misidentified the crumpling of paper as a rubber band snapping" the snapping of fingers and the clapping of han ls as metallic sounds and the sound of a coin being dropped on a desk as a heavy metal sound Gross clinical testing of sound localization, with patient s eyes covered using loud finger snaps and the clang of a spoon against a metal basin, exhibited highly inaccurate responses in the entire auditory field. Although indicating he clearly heard the sound each time he was able to lat ralize the sound no better than would be expected by chance guessing. The patient had never been able to read music had never played a musical instrument and stated he had never been able to carry a tun or sing well. On testing, he was able to sing crudely several songs of his choice and several songs given him by title He was able to repeat phrases of songs sung to him and to hum along with songs being played on the radio. Neither at the time of this examination nor at any other time during his hospitalization was there any evidence of apraxia.

Te ts f hearing

The patient had had a normal pure-tone air-conduction audiogram in August 1963 prior to his induction into military service (Fig. 4 A) On the day of his second admission, pure-tone air-conduction audiometry showed a 60 to 85 dB loss at all frequencies in both ears (Fig. 4 B) Pure-tone bone-conduction audiograms at the time of this examination and on all subsequent examinations closely corresponded t the air conduction results, confirming the clinical impression of sensorineural impairment Serial audiometric testing was accomplished during the second hospitalization. Two representative audiograms from this period of recovery are shown (Fig 4 C and 4 D) There was a gradual improvement in hearing sensitivity in both ears, the most rapid improv ment occurring at the speech frequencies. A considerable loss at the high frequencies persisted in the *right* ear throughout the period of testing and wa still present three months after admission.

Békésy udiometry was attempted shortly after admission but produced uch wide excursion that it was felt to be invalid At the same time electrodermal udiometry was accompli hed. No response was obtained at any frequency even at high sound levels, thus confirming the marked hearing loss. Delayed Speech Feedback testing was carried out one week after admission. A Lombard-type response was observed when the feedback was 30 dB HL binaurally There was also a change in reading rate Similar changes were bserved when the feedback was at 60 dB HL in the left ear only and at 70 dB HL in the right ear only

Speech audiom try was carried out on 3 June 1968 aft r pure tone heari g in the speech frequencies had returned to near-normal levels and

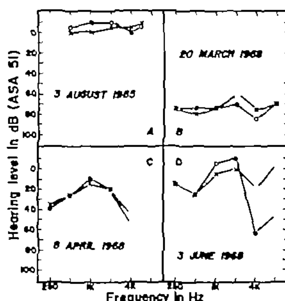


Fig. 4 Pure tone air conduction audiograms. o–o = Right ear x–x = left ear (ASA-51) (A) Prior to onset of illness (3 August 1965) exhibiting normal hearing at all frequenci s in both ears. (B) On day f second admissi n (20 March 1968) e hibiting marked he ring l ss at all frequencies bilaterally (C nd D) During recovery phase second admi sion (8 April 1968 nd 3 Ju 1968) hibiting in both ears a return toward nor m l, especially at speech frequencies, with persistent marked l ss at high frequencies in right r

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III PSYCHOACOUSTIC FINDINGS

Introduction

In order to highlight abnormalities in psychoacoustic performance data, every procedure administered to our patient was also administered to a normal control subject. The latter was a 25-year-old male with normal hearing and no history or evidence of CNS disorder

For purposes of comparison the patient is hereinafter referred to as the experimental subject, or simply "E" The normal is hereinafter referred to as the control subject, or simply "C" All of the findings subsequently reported in this monograph, for both E and C, were obtained during the month of June 1968 The following sections compare performance of E and C on listening tasks involving pure-tone audiometry speech intelligibility loudness discrimination and auditory temporal order

Pure tone audiometry

Fig. 5 compares audiograms of E and C obtained by conventional manual technique C showed relatively normal sensitivity at all test frequencies, but E continued to show the high frequency loss, greater on the right ear illustrated in the audiogram of 3 June 1968 (Fig. 4 A) The sensitivity loss had apparently stabilized, and the threshold configuration was reasonably reliable

Fig. 6, on the other hand, compares manual and Békésy audiometric threshold on E. We note a striking difference between thresholds obtained by the two techniques. On the left ear result are reasonably equivalent by either technique On the right ear however the Békésy thresholds are

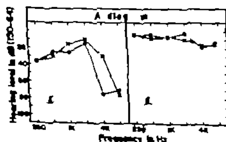


Fig. 5.

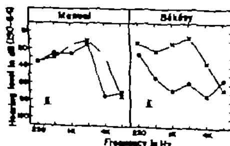


Fig. 6.

Fig. 5. Air-conduction audiograms of E and C obtained by conventional manual technique (J ne 1968)

Fig. 6. Comparison of manual and Békésy air-conduction thresholds in subject E.

when there was no significant speech frequency loss in accordance with the criteria of Street (1957). Spondee threshold testing yielded no accurate responses in the right ear and a threshold hearing level of 16 dB in the left ear. PB discrimination testing at 40 dB SL (above spondee threshold) yielded 0% in the right ear and 36% in the left ear. PB discrimination was retested on the left ear at sensation levels between 10 and 80 dB and yielded the following scores: 10% at 10 dB, 16% at 20 dB, 24% at 30 dB, 36% at 40 dB, 16% at 50 dB, 4% at 60 dB, 0% at 70 dB and 0% at 80 dB.

Electronystagmography

An electronystagmographic examination was carried out by Dr A. C. Coats, Baylor College of Medicine, on 18 June 1968. Caloric responses showed a directional preponderance to the right which was well outside normal limits. There was no significant unilateral weakness. The optokinetic response was of normal form and showed no significant asymmetry. No spontaneous, gaze, or positional nystagmus was observed.

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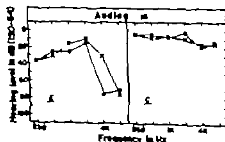


Fig. 5.

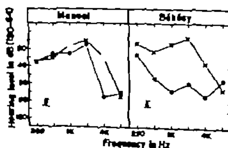


Fig. 6.

Fig. 5. Air-conduction audiograms of E and C obtained by conventional manual technique (June, 1968)

Fig. 6. Comparison of manual and Békésy air-conduction thresholds in subject E.

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Electronystagmography

An electronystagmographic examination was carried out by Dr A C. Coats, Baylor College of Medicine, on 18 June 1968 Caloric responses showed a directional preponderance to the right which was well outside normal limits. There was no significant unilateral weakness. The optokinetic response was of normal form and showed no significant asymmetry No spontaneous, gaze or positional nystagmus was observed

III PSYCHOACOUSTIC FINDINGS

Introduction

In order to highlight abnormalities in psychoacoustic performance data, every procedure administered to our patient was also administered to a normal control subject. The latter was a 25-year-old male with normal hearing and no history or evidence of CNS disorder

For purposes of comparison the patient is hereinafter referred to as the experimental subject, or simply E' The normal is hereinafter referred to as the control subject, or simply C' All of the findings subsequently reported in this monograph, for both E and C, were obtained during the month of June, 1968 The following sections compare performance of E and C on listening tasks involving pure-tone audiometry speech intelligibility loudness discrimination and auditory temporal order

Pure tone audiometry

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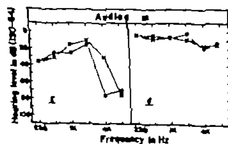


Fig. 5

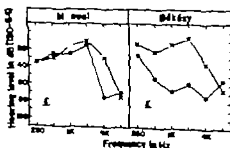


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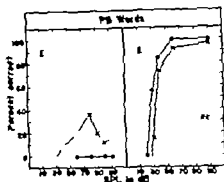


Fig. 8

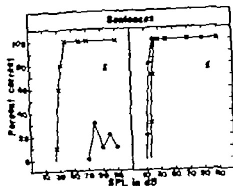


Fig. 9

Fig. 8. Performance-intensity (PI) functions for monosyllable (PB) word lists.

Fig. 9. Performance-intensity (PI) functions for synthetic sentence identification (SSI) lists.

Although this situation rendered conventional spondee threshold testing ambiguous, we attempted to determine at least a rough approximation by repeated presentation of the single spondee word "cowboy". Spondee identification thresholds, or more properly "cowboy" thresholds obtained in this fashion were 20 dB HL for the left ear and 66 dB HL for the right ear. The 20 dB level for the left ear agrees quite well with the average pure tone hearing level of 18 dB. On the right ear, however, the threshold for "cowboy" was 44 dB poorer than the average pure-tone hearing level by manual audiometry but corresponded well to the average pure-tone hearing level by Békésy audiometry (61 dB).

We turned next to a synthetic sentence identification (SSI) task (Jerger *et al.* 1968). Fig. 9 shows PI functions of both subjects for sentences presented in quiet. C's performance rose rapidly to 100% correct on both ears. E's performance on the left ear illustrated the unique improvement typically found for sentence materials. Although his maximum PB score was only 36%, sentence identification scores were 100% at approximately 40 dB SPL and above. On E's right ear, however, the maximum sentence identification score was only 30%. The pattern of the PI function *for sentences* on the right ear closely resembled the pattern of the PI function for PB words on the left ear. Similar maxima and a "roll-over" *effect* at intensities greater than 80 dB SPL were noted. Apparently E could not take advantage of the additional contextual clues and redundancy of the sentence message set on the right ear. E *stated that* sentences presented to this ear sounded like "short wave radio". He stated that occasionally he heard speech, but that "the rest of it is buzz". On further questioning he said that the speech sounded like two voices, one high and one low. He could understand the high voice but the low voice *muffled* what he could hear.

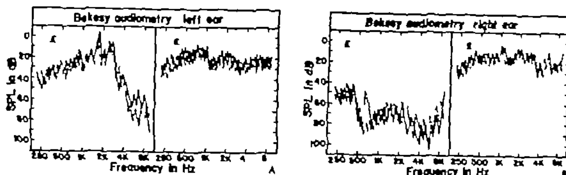


Fig. 7 Comparison of Békésy audiograms of E and C (int —, cont) (A) Left ear (B) Right ear

substantially poorer than the conventional manual thresholds over the range from 500 to 2000 Hz The Békésy thresholds plotted in Fig. 6 were obtained on a standard Békésy audiometer (Grason–Stadler model E 800) Frequency changed at the rate of one octave/min, intensity changed at the rate of 2.5 dB/sec, and the signal was periodically interrupted at the rate of 2 5 i p s

We believe that the threshold differences between manual and Békésy results on the right ear may be accounted for by differences in the on duration" of signal presentation under the two methods For Békésy audiometry the on-duration was approximately 200 msec, whereas for manual audiometry the on-duration of each signal was typically greater than one second In chapter V we present data indicating that, in E s right ear 200 msec is an insufficient duration to reflect maximum sensitivity

Fig 7 compares actual Békésy tracings of E and C on left and right ears In all cases we note a type I tracing (Jerger 1960 c) Thresholds for con tinous and interrupted tones overlap There is no evidence of the excessive adaptation to sustained stimulation characterizing eighth nerve and brain stem disorders

Speech audiometry

Fig. 8 compares E and C on performance-intensity (PI) functions for lists of 25 monosyllabic (PB) words. The PI function for E's left ear rises to a maximum of 36% then falls off rapidly as speech intensity is increased On the right ear there is no response to PB words at any level

It has been previously noted to be sure that impaired speech intelli gibility in the presence of relatively normal sensitivity is characteristic of central auditory disorders, but in this patient the discrepancy between sen sitivity and intelligibility is particularly dramatic especially on the right ear In spite of the average pure tone hearing level (500–2000 Hz) of 22 dB the PB score was 0% In response to PB words E stated that he heard only a buzz in the right ear

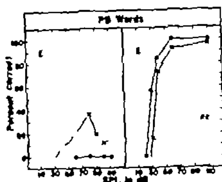


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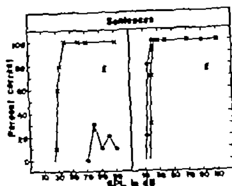


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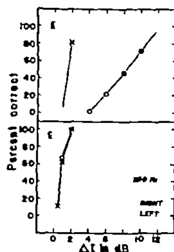


Fig. 10

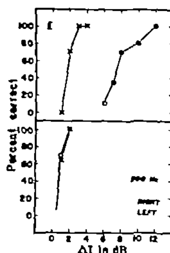


Fig. 11

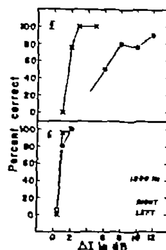


Fig. 12

Fig. 10. Psychometric functions for discrimination of loudness change at 250 Hz.

Fig. 11. Psychometric functions for discrimination of loudness change at 500 Hz.

Fig. 12. Psychometric functions for discrimination of loudness change at 1000 Hz.

Loudness discrimination

The ability to detect small changes in sound intensity was measured by the quantal psychophysical method (Stevens *et al.*, 1941). Short intensity increments were added to a steady state pure-tone signal at aperiodic intervals. Each subject responded by pushing a button whenever he detected a change in the loudness of the steady tone. Increment duration was 200 msec, with a rise-decay time of 25 msec. The interval between successive increments was either 2, 3 or 5 sec determined by a random schedule. Each of the three intervals occurred with equal probability. Increments were presented in blocks of 20. Increment size was constant within each block, but varied over successive blocks in order to construct psychometric functions over the response range from 0 to 100% correct detection. The SPL of the steady state signal was held constant at 90 dB for four test frequencies: 250 Hz, 500 Hz, 1000 Hz and 2000 Hz.

Fig. 10 shows results at 250 Hz for both right and left ears of E and C. We note that C reaches 100% correct detection on either ear for an intensity increment (ΔI) of only 2 dB. Subject E does almost as well as C on the left ear but the psychometric function for the right ear reflects dramatically poor loudness discrimination. An intensity increment of 12 dB is required to reach 100% correct detection.

Fig. 11, 12 and 13 show analogous results at 500, 1000 and 2000 Hz. The pattern of results illustrated in Fig. 10 is repeated. E performs about as well as C on his left ear but shows relatively poorer loudness discrimination on his right ear.

Fig. 14 shows results at 1000 Hz when ΔI is held constant at 1 dB, and the

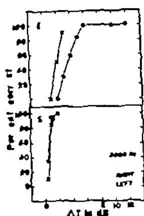




Fig. 13 Fig. 14.

Fig. 13. Psychometric functions for discrimination of loudness change at 2000 Hz.

Fig. 14. Loudness discrimination as function of signal level for ΔI = 1 dB.

SPL of the steady-state carrier tone is varied (the paradigm of the SISI test). C reaches 100% correct detection at an SPL of 80–90 dB. E never does reach 100% detection, but attains a maximum of 80% on the left ear at about 90 dB SPL. On E's right ear, however, performance never exceeds 10% even at 110 dB SPL.

These results are in accord with Hodgson's (1967) observations on a patient with left hemispherectomy. Hodgson noted reduced SISI scores at high intensity levels on the ear opposite the affected side of the brain. We are unable, however, to reconcile these findings with Swisher's (1967) report of bilateral hypersensitivity to intensity change following left temporal lobe excision. The hypersensitivity was observed post-operatively but not pre-operatively. Measurement was, unfortunately, confined to 2000 Hz, a frequency at which the present results show a minimum difference between E's left and right ears.

Temporal order

Temporal ordering refers to the patient's ability to identify the order in which different auditory events occur in time. The phenomenon is of particular interest here because of Efron's (1963) recent report that the capacity to order temporally distinct events may be profoundly disturbed in aphasic patients, especially those of the expressive variety, and because of the findings of Hirsh and Sherrick (1961) that the minimum temporal separation required for correct ordering is remarkably independent of sense modality in the normal subject.

Unfortunately, Efron, in his study of aphasics, and Hirsh and Sherrick, in their study of normals, used distinctly different signal configurations.

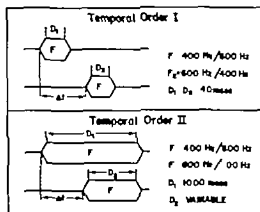


Fig. 15.

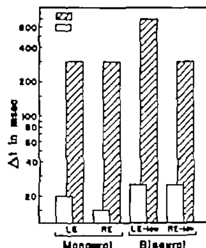


Fig. 16

Fig. 15 Two perimental paradigms for the measurement of t mp ral rder

Fig 16. Results f r temporal order mea ured by paradigm I nd method of limits.

In order to gather data suitable for comparison with both studies, therefore we found it necessary to measure temporal order by two methods.

Fig 15 illustrates the two different signal configurations employed Paradigm I is roughly analogous to Efron s paradigm although there are differences in detail Efron s signals were pulses at frequencies of 250 and 2500 pps presented for 10 msec, whereas we used tones of 400 and 600 Hz presented for 40 msec Paradigm II is analogous to the paradigm of Hirsh and Sherrick The principal difference is that while they used a 500 msec duration for the longer tone, we found it necessary to increase the duration to 1000 msec, in order to accomodate the extraordinarily large temporal separations required by E for correct identification of order From the listener s standpoint the crucial difference between paradigms I and II is that in I both onset and termination of F_2 vary as a function of Δt whereas, in II only the onset of F_2 varies Both tones end simultaneously Paradigm I thus provides at least two separate clues to order whereas paradigm II provides only one

For both paradigms testing was carried out by a method of limits technique Signal pairs were presented at 8 sec intervals at an SPL of 80 dB After each pair had been presented the subject indicated verbally whether the first or leading tone was the high pitched or the low pitched member of the pair The actual assignment of high or low pitched tones as the leading signal was randomly varied over successive presentations with the *a priori* constraint of equal probability Following a method of limits technique the size of Δt was both decreased from an easily identified point and increased from zero difference until descending and ascending limens had been defined The midpoint between these two points was defined as the

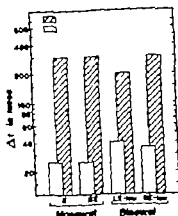


Fig. 17

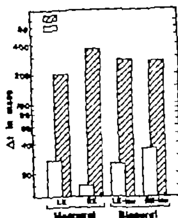


Fig. 18.

Fig. 17 Result for temporal order measured by paradigm II and method of limits.
Fig. 18 Result for temporal order measured by paradigm II and 2AFC method.

minimum separation for temporal order (Δt) and is so labelled on subsequent figures.

Fig. 16 shows results obtained under paradigm I for both monaural and binaural presentations In the monaural conditions both tones were presented t the same ear In the binaural conditions the lower of the two pitches always went t one ear and the higher to the other We see in Fig. 16, striking confirmation of Efron s findings. Whereas C can resolve temporal order in 10–25 msec E requires substantially larger temporal separation, in the range from 300 to 600 msec. The logarithmic display of Δt necessary to encompa s results for C and E in the same figure actually minimizes the di parity between the two subjects. A linear plot of Δt would more effec tively dramatize the difference

Fig. 17 shows results obtained under paradigm II Here E does somewhat better than under paradigm I, but Δt is never less than 200 msec under any condition. Subject C, on the other hand, never requires more than a 40 msec separation

In rder to en ure that E' performance was not confounded by the exact psychophysical procedure (limits) employed to define Δt the entire set of measures h wn in Fig. 17 was repeated using a two-alternative, forced-choice (2AFC) technique. Over blocks of 20 signal pairs Δt was hel l constant, and either the higher or lower pitch occurred as the leading sound with random but equal probability The size of Δt was varied over successi e block to define a complete psych metric function The threshold for temporal rder was defined as the 75% point of this function. Results are hown in Fig. 18 We can see no important differences relating to type of psychophysical method employed

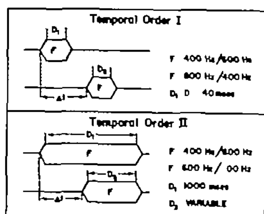


Fig. 15.

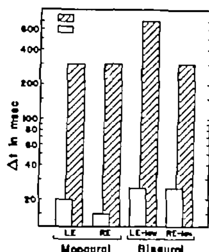


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pairment in temporal pattern discrimination after bilateral ablation of auditory cortex.

It is also noteworthy that E's impairment in temporal ordering does not show the ear specificity previously demonstrated for both speech intelligibility and loudness discrimination. In both of these areas results for the right ear were uniformly poorer than results for the left ear. In temporal ordering tasks, however, we can see no consistent differences among right ear, left ear or binaural results.

It is of some interest to ask, therefore, whether E's performance is a manifestation of some more general loss in sequential discrimination not specific to auditory signals. To this end, we investigated temporal order for visual events. Two 12 volt light bulbs, each approximately 1 cm in diameter, were mounted horizontally in a box 5 inches high and 6 inches long. The horizontal separation between bulbs was 1.5 inches. One bulb had a red shield, the other a green shield. Subjects were seated approximately 1 meter from the visual array. Temporal intervals between light signal onsets were varied according to paradigm II, and the subject responded either "red-green", "green-red" or "same". Thresholds were defined by a method of limits technique. There was no difference between C and E on this task. Both subjects correctly ordered visual signals at a temporal separation of 20–30 msec. We conclude, therefore, that E's temporal ordering deficit is a specifically auditory impairment.

Summary

Approximately three months after this patient's second cerebral insult auditory sensitivity, as measured by conventional manual audiometry, had returned to relatively normal levels in the region below 2000 Hz. Above this point, however, a bilateral high frequency loss, somewhat more severe on the right ear, persisted.

In contrast to the bilateral symmetry suggested by the manual results, Békésy audiometry revealed substantially poorer sensitivity on the right ear. Both ears showed type I tracings.

Performance-intensity functions for phonetically balanced (PB) word lists showed extremely impaired speech understanding on both ears, with poorest performance on the right ear. Performance-intensity functions for synthetic sentences (SSI) were normal on the left ear but severely impaired on the right ear.

Loudness discrimination, as measured by the quantal psychophysical method, was normal on the left ear but severely impaired on the right ear.

Perception of auditory temporal order was severely impaired in both ears. Whereas the control subject could correctly order events differing by 10–40 msec, the experimental subject required temporal delays of 200–[illegible]00 msec for successful performance. The effect was invariant over two test paradigms and two psychophysical methods. The perception of temporal order for visual events was unimpaired.

Table 1 *Temporal order thresholds (Δt in msec) of experimental (E) and control (C) subjects for four different frequency pairs*

Data obtained by paradigm II and method of limits.

Frequency pairs	Subject	Monaural		Binaural	
		LE	RE	LE low	RE low
400– 600 Hz	E	300	300	300	300
	C	25	25	40	35
800–1200 Hz	E	300	400	CNE*	350
	C	25	20	35	40
2500–3500 Hz	E	600	CNE*	CNE*	CNE*
	C	20	20	35	35
500–2000 Hz	E	250	250	300	250
	C	20	20	25	25

* Could not establish (see text)

In order to determine the generality of these differences across the frequency range additional data were gathered by the method of limits for frequency pairs of 800–1200 Hz, 2500–3500 Hz, and 500–2000 Hz. The latter pair was included in order to ensure that E's poor performance was not the result of inability to resolve the approximately one-half octave pitch differences used to this point.

Table 1 summarizes values of Δt obtained for these various frequency combinations. Entries labelled "CNE" indicate conditions under which E could not order the two events correctly even with a temporal separation in excess of 800 msec. In these conditions he insisted that he heard only a series of pulses followed by a tone. When the signals were presented binaurally he heard pulses on the left ear and tone on the right ear. The pulses always preceded the tone.

The data of Table 1 reveal a consistent impairment in temporal resolution across the frequency range present even when the pitch difference is two octaves (500–2000 Hz). Furthermore, comparison of Fig. 16 and 17 reveals, that the effect is largely independent of the exact methodology employed to measure temporal order.

These results are entirely consistent with the previous findings of Efron (1963) and Edwards and Auger (1965) on patients with unilateral hemispheric lesions. Efron, for example, obtained Δt's ranging from 150–350 msec in patients with receptive aphasia and from 150–700 msec in patients with expressive aphasia. As noted earlier (*Chapter II*) our patient E, showed some aphasic symptoms following his initial cerebral accident but was largely symptom free at the time of this testing. The present results are also consistent with recent findings in animals. Jerison and Neff (1953), Diamond and Neff (1957), Neff (1961) and Wegener (1968) all report im

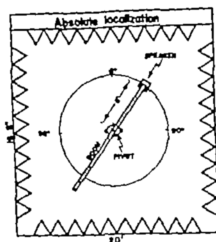


Fig. 19 Arra gement of pparatus for the measurement of absolut sound localization. Subject i seated, blindf lded, i the center of anechoic hamber A loudspeaker is mounted on boom t radius of 8' from the center of the ubject head.

(1956) and Butler *et al* (1967) also found a decline in localization accuracy in the vicinity of 2000 to 4000 Hz.

For subject E sound localization accuracy was consistently poor for all signals. Errors as large as 180 were observed. In addition, we did *not* find the improved localization accuracy f r sawtooth noise and click signals that we observed in the control subject. As seen in Fig. 20 the two judgement that were obtained at each azimuth were occasionally quite dif ferent For example in Fig 20 E, when the sound source was presented at 30 on the left, E responded "right 45 on the first trial and left 90 " on the second trial Subject E olunteered that 4000 Hz was more difficult to localize than either 400 Hz or 1000 Hz. He stated that the 4000 Hz signal tarts out unding like a buzz, then smooths off into a high-pitched sound"

A y r f und disturbance f sound localization ability has been reported previ u ly in animals with bilateral temporal lobe ablations (Neff Arnott, and F her 1950 Neff Fisher Diamond and Yela, 1956 Neff 1961 Masterton and Diamond 1964 Wegener 1968) In addition, a few patients with bilateral hemispheric lesion have been studied and were found to ha a severe r total loss of sound localization ability (Weber 1947 Sanchez l ng and F rster 1958)

Fig. 21 ummarizes non-directional error in sound localization for both subjects. For each signal the discrepancy between actual and apparent location f the sound was averaged acro both trials at all 13 azimuths. F r thi analysi errors were averaged without regard to their direction This a er ge err is, theref re non-directional

F r ubject C n n-directional errors for pure tone signal became larger

IV AUDITORY LOCALIZATION

Absolute locali ation

In order to study the absolute localization of actual sound sources in space a loudspeaker was mounted on a boom and pivoted so that it travelled the perimeter of a circle 16 feet in diameter (Fig. 19) The path of the loudspeaker was calibrated in 1 steps.

Testing was conducted in an anechoic chamber (20 feet by 16 feet 8 inches) The subject was seated in a dental chair at the center of the circle 8 feet from the sound source The height of the subject s chair was adjusted so that the tragus was in the same horizontal plane as the center of the loudspeaker cone The headrest of the dental chair was then adjusted so that the subject s head fit comfortably into it The subject was instructed to maintain this head position throughout each experimental run No further attempt was made to restrict head movement During all test conditions, the subject wore a blindfold

Localization of pure tone click and sawtooth noise signals was tested at 15 intervals from 90 left to 90 right (see Fig 19) For each signal presentation the subject verbally reported the perceived location of the sound to the nearest 5 interval Two separate judgements were obtained at each test azimuth Signals were presented at 60 dB SL. For sawtooth noise and pure tone signals, duration was 10 sec with 100 msec rise-decay time For click signals, a click train with a repetition rate of 2 clicks per sec was presented for a total duration of 10 sec The train was generated by rectangular pulses of 1 msec duration

Fig. 20 presents results for both subjects as a function of signal azimuth for clicks (*a*) sawtooth noise (*b*) 400 Hz (*c*) 1000 Hz (*d*) and 4000 Hz (*e*) Data are reported as apparent or perceived azimuth in degrees. The diagonal line represents perfect agreement between the actual location of the sound source and the subject s perceived location.

For subject C, localization was most accurate for click and sawtooth noise signals As seen in Fig. 20 A and 20 B all responses cluster around the line representing perfect agreement This finding is consistent with previous studies of sound localization in space (Stevens and Newman 1936 Sandel *et al* 1955) For example Stevens and Newman reported that subjects localized noi es more readily than pure tone signals

Subject C s precision in localizing pure tone signals varied as a function of frequ ncy Localization errors were reasonably small at 400 Hz and 1000 Hz, but became noticeably larger at 4000 Hz Stevens and Newman

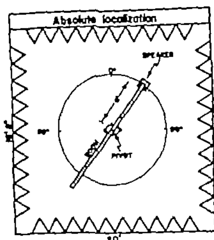


Fig. 19 Arrangement of pparatus for the measurement f absolut sound localization. Subject i seated, blindf lded, i the center f nechoi hamber A loudspeaker i mounted on boom t radius of 8' from the center f the ubject head

(1930) and Butler *et al* (1967) also found a decline in localization accuracy in the vicinity of 2000 to 4000 Hz.

For subject E sound localization accuracy was consistently poor for all signals Errors as large a 180 were observed. In addition, we did not find the improved localization accuracy for sawtooth noise and click signals that we observed in the control subject As seen in Fig. 20 the two judgement that were obtained at each azimuth were occasionally quite dif ferent F r example in Fig 20 E, when the sound source was presented at 30 on the left, E responded right 45 on the first trial and left 90 on the second trial. Subject E volunteered that 4000 Hz was more difficult t localize than either 400 Hz or 1000 Hz. He stated that the 4000 Hz signal tart out unding like a buzz, then mooths ff into a high pitched sound"

A pr f und disturbance f sound localizati n ability has been reported previou l in animals with bilateral temporal lobe ablation (Neff Arnott, and Fi her 1950 N ff Fisher Diamond and Yela, 1956 Neff 1961 Masterton a d Diamond 1964 Wegener 1968) In addition, a few patients with bilateral hemispheric lesions ha been studied and were found to ha e severe r t tal loss f sound localization ability (Weber 1947 Sanchez Long and Forster 1958)

Fig 21 umm rizes non-directional error in sound l calization for both ul jects. For each signal the discrepancy between actual and apparent location f the sound wa averaged acros both trials at all 13 azimuths. For thi a alysis errors were averaged without regard to their direction. This av rage err r is, tl eref re n n-directional

F r subject C non-directional errors for pure t ne signals became larger

IV AUDITORY LOCALIZATION

Absolute localization

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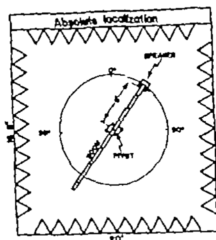


Fig. 19. Arrangement of pparatus for the mea rement of beolut sound localization. Subject is seated, blindf lded, in the center of nechoic chamber A loudspeaker I mounted boom at radius of 8' from the center f the ubject head.

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Fig. 21 summarizes non-directional error in sound localization for both subjects For each signal the discrepancy between actual and apparent location f the sound was averaged across both trials at all 13 azimuths. For this analysis errors were averaged without regard to their direction. This a erage erro is, therefore n n-directional.

For s bject C non-di ectional errors for pure tone signals became larger

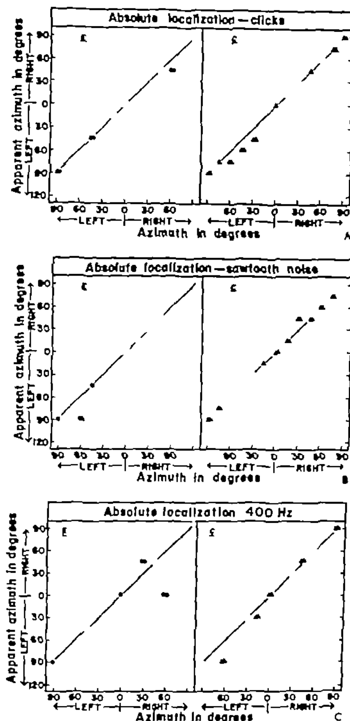
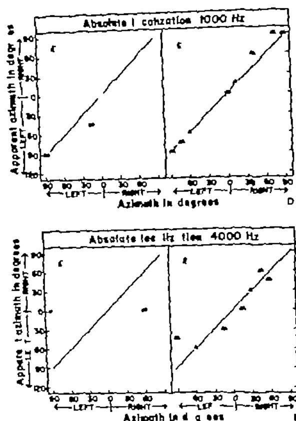


Fig. 20 Absolut judgem nt f sound location t 13 azimuth varvi g from 90 R t 90 L. (A) Cli k trains, (B) sawtooth noise (C) 400 Hz, (D) 1000 Hz, (E) 4000 Hz.

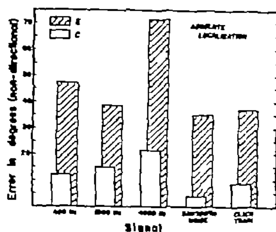
as frequenc\ increased As shown in Fig. 21 the average errr r was approxi mately 13 at 400 Hz, 10 at 1000 Hz, and 21 at 4000 Hz. These data closel\ correspond to the findings of Stevens and Newman (1934) for lo-calization of pure t nes in the horizontal plane They reported an average error of approximatel\ 12 at 400 Hz, 13 at 1000 Hz, and 20 at 4000 Hz.



Subject C's average non-directional error for click and sawtooth noise signal illustrates the fact that complex sounds are more accurately localized than pure tones. The average localization error was only 4 for sawtooth noise and 8.6 for click trains. These data are in accordance with the findings of Stevens and Newman (1936) and Sanchez-Longo and Forster (1958).

Results for E also showed a relation between error and signal frequency. Localization accuracy was poorest at 4000 Hz. Although errors were unusually large for all sound sources, the average error at this frequency was 71. Average errors for other test signals were reasonably constant, ranging from approximately 36 to 49. These results again dramatically illustrate the marked difficulty in sound localization experienced by E.

Fig. 22 summarizes directional error or bias, in sound localization for both subjects. For this analysis the direction of the discrepancy between actual and apparent location of the sound was taken into account. This average error is, therefore, directional in the sense that it reflects systematic directional bias in localization. For subject C there was a consistent directional error to the left. Although this bias was small, less than 10 for



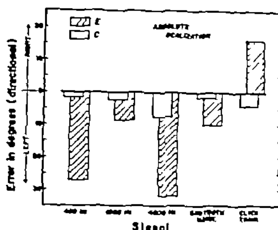


Fig. 21 Non-directional error in absolute localization, a eraged across trials nd azimuths, for all signals.

Fig 22 Directional error in absolute localization, averaged acro tri ls and azim ths, for ll ignals.

all signals, apparent locations tended to be left of the test azimuth With the exception of click signals, a consistent bias to the left was also observed for subject E. The directional error for this subject was small for 1000 Hz and sawtooth noise signals. Although the average non-directional error for these signals was large approximately 36 to 40 the directional error was only about 10 A large bias to the left approximately 26 to 31 was found at 400 Hz and 4000 Hz. Curiously a bias of 16 to the right was found for click signals

Fig. 23 shows non-directional error averaged across all signal sources as a function of signal azimuth Fig. 24 shows the analogous average direc tional error as a function of azimuth As seen in Fig 23 C's performance was most accurate in the region directly in front of the subject or 0 azi muth Stevens and Newman (1936) also found that localization errors were smallest for sounds in the median plane The average non-directional error of subject C ranged from approximately 6 to 12 in the right auditory field There was curiously poor performance between azimuths of 15 and 60 in the left field In this range the average non-directional error was approximately 15 to 22 For subject E accuracy was poor at all azimuths. The average non-directional error ranged from 27 to 69 In contrast to C, the most accurate judgements were obtained at 45 on the left Accuracy became progressively poorer as the test azimuth moved away from this point

In general, directi nal err rs for C seen in Fig 24 showed a left bias for signals presented in the left auditory field and a right bias for signals in the right audit ry field However the opp site effect was seen for signals presented at 90 azimuth Apparently C judged signals presented at 90

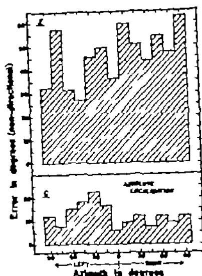


Fig. 23.

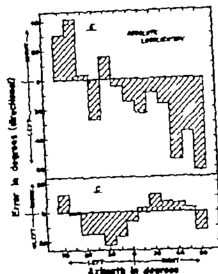


Fig. 24.

Fig. 23. Non-directional erro l absolut localization, veraged across trial nd signal conditions, as f ncti of azimuth

Fig. 24. Directional error in bsolute localization, veraged across trials nd signal condi tions, function of azimuth.

to be more medially located Butler *et al* (1967) also found that judgements for sound originating at the most peripheral positions were displaced toward the median plane For subject C, judgements in th right auditory field were more accurate than judgements in the left field In addition, there was a slight bias to the left for signals presented at 0 Directional errors were how ver generally small Directional errors for subject E were smallest for judgements from approximately 30 on the left to 30 on the right. In addition there was a bias to the left for all judgements from 15 in the left auditory field to 90 in the right field. The magnitude of the directional error increased dramatically as the test azimuth moved to 90 on the right Apparently sounds were generally per cei ed in the median plane or left auditory field even though signals were presented at the extreme right periphery We see also the curious bias to the rigt t for signals presented in the extreme left periphery that was observed in the control subject Appar ntly for both subjects, test signals presented at 90 in either field were usually judged t be more medially located.

Finally in order to ensure that E's poor performance on sound localization tasks wa not confounded by the verbal response mode employed, th ent re procedure for click trains was repeated with the addition of a purely motor response In addition to his verbal report E was instructed to point, with a yardstick, to the apparent sound location. This modifica-

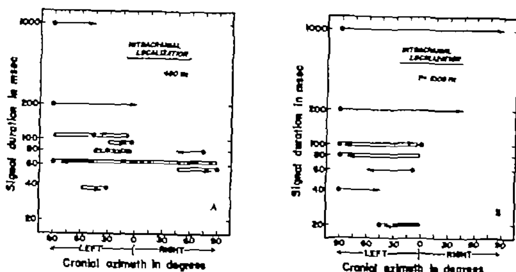


Fig. 25 Effect of signal duration in intracranial localization f r subject E. (A) 400 Hz, (B) 1000 Hz.

tion in procedure had no effect on performance There was little discrepancy between verbal report and indication by pointing, and accuracy of localization was not improved

During this procedure however F startled us by asking, Should I point to where the sound begins or where it ends?" Upon further questioning E reported that sounds "moved" during the 10 sec presentation interval Consistent judgements were difficult because signals were never still"

Intracranial localization

In further pursuit of this traveling sound phenomenon, signals were presented binaurally to E through earphones, and intracranial localization was studied as a function of signal duration

A single pure-tone signal was split and delivered to matched, phased earphones at equal SPL (80 dB) Signals were presented once every 2 sec at on-durations ranging from 20 to 1000 msec The rise-decay time of each signal was 5 msec After each signal presentation E was asked to report the perceived location of the sound along an arc from ear to ear The arc was divided into two quadrants from midline to left ear level (0 to L 90) and midline to right ear level (0 to R 90) The subject reported location in respective quadrants in 15 steps

Fig. 25 shows results at 400 Hz (a) and 1000 Hz (b) At 400 Hz, two judgements were obtained for on-durations between 20 and 100 msec For all other signal presentations only one judgement was obtained As shown in Fig. 25 the perceived movement of sounds with on-durations between 20 and 100 msec appears to be random Apparently sounds travelled in both directions and occasionally in an oscillatory manner For example in Fig. 25 A, at an on-duration of 60 msec E reported that the sound began

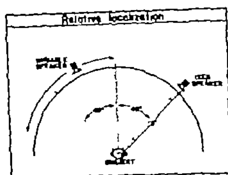


Fig. 26. Arrangement of apparatus for the measurement of relative sound localization.

at L 90 rotated over to R 90 and then rotated back to L 90 Perceived movement of sounds with on-durations greater than 100 msec was consistent at both 400 and 1000 Hz. All perceived sounds initially appeared to be on the left side at 90 then travelled to the right.

This anomalous finding has considerably significance for the interpretation of all the sound localization data. It is considered in further detail, in chapter V Critical On-Time"

Relative localization

Another aspect of auditory localization is the precision with which a subject can equate the azimuth of a signal in one field with the azimuth of a different signal in the opposite field. In distinction to the absolute judgement of azimuth this may be termed relative localization

Fig. 26 shows the arrangement of the experimental apparatus used to measure the precision with which subjects E and C could localize the relative positions of two different sounds. The situation was identical to the arrangement for absolute localization, except that a second loudspeaker was added The latter was mounted on a rigid stand and fixed at specified azimuths from 0 to 90 in one auditory field The original loudspeaker mounted on the boom, could be placed at various azimuths in the opposite field.

Testing proceeded by positioning the fixed loudspeaker at a particular azimuth in one field, positioning the variable loudspeaker at a randomly selected azimuth in the opposite field, then alternately presenting a 400 Hz signal to the fixed speaker and a 600 Hz signal to the variable speaker The duration of each signal was 1.25 sec with a rise-decay time of 100 msec. Signals were alternated automatically between speakers at the rate of one alternation each 2.5 sec. Signals were separately adjusted to 60 dB SPL. A single trial consisted of a 10 sec presentation of the alternating signals. After each trial the subject's task was to report whether the azimuth of the 600 Hz signal from the variable loudspeaker was to the left, to the

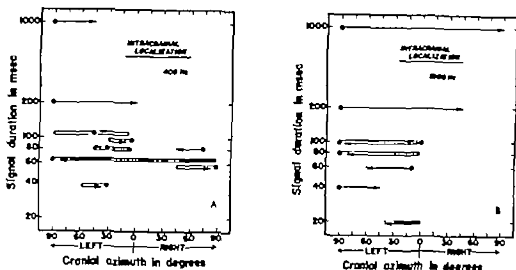


Fig. 25 Effect of signal duration in intracranial localization for subject E. (A) 400 Hz, (B) 1000 Hz.

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Table 2. *Visual perception of angles (error in degrees)*

Subject	Vertical	Horizontal
E	1.25 L	1.0 L
C	1.20 L	1.0 L

speaker was placed at 0 and 15 on the left. Judgements at all other test azimuths were approximately 70 to 80% correct. The average percent correct response at all test azimuths for this subject was 81% In contrast, subject E's performance was quite poor E achieved only 48% correct for all azimuths. Like C, however E's performance was best for judgements in the median plane, or 0 Mills (1958) also found that performance was most accurate in the region straight ahead of the subject for judgements of minimum audible angle

Performance as a function of test azimuth can be seen more clearly in Fig. 28 These results were obtained by averaging performance in the right and left auditory fields at each azimuth. For both subjects, performance was best for signals presented at 0 Then accuracy systematically decreased as the test azimuth increased toward 75 C's responses ranged from 100% correct at 0 to 72% correct at 75 E's responses however were unusually poor ranging from approximately 60% at 0 to 40% at 75 These results, while poorer than C's are well above the chance performance level (33%) The importance of these results lies principally in what they do not show We fail to see evidence, in E's performance of any systematic differences between fields or among azimuths. His pattern of performance is similar to C's but displaced downward considerably

Finally in order to ensure that E's performance on the relative localization task was specifically auditory and not the result of a more generalized deficit in the judgement of angles, the following procedure in visual perception was carried out. A circular disc, 38 inches in diameter was mounted on a tripod with the center 47 inches from the floor approximately eye level for the subject. A pointer 20 inches long and 1 inch wide was pivoted in the center f the disc. The disc was painted dull black, the pointer white The subject was seated approximately 6 feet from the visual target in the darkened anechoic chamber The tester moved the pointer until the subject judged the angle formed between the pointer and a point at 9 o clock on the disc to be vertical (90) or horizontal (180) For vertical judgements, responses were obtained with the pointer moving from the left and from the right. The back of the disc was calibrated in 1 steps. After each judgement, the error in degrees to the right or to the left of the test angle was recorded.

Table 2 shows the error in degrees for each subject s judgement of vertical and horizontal angels. Both subjects performed within the normal range.

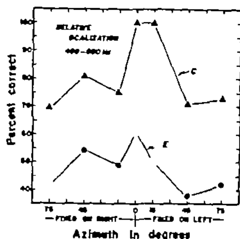


Fig. 27

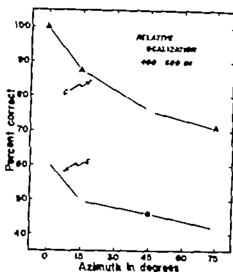


Fig. 28.

Fig 27 Percent correct localization f variable speaker a a function of target azimuth.
Fig. 28 S me data a Fig 27 but result averaged across fields.

right or identical with the target azimuth of the 400 Hz signal If for example the 400 Hz signal was placed at an azimuth of 45 in the right field and the subject felt that the 600 Hz signal was at an azimuth of 45 in the left field then he would respond same If he felt that the azimuth of the 600 Hz signal was less than 45 he would respond right" indicating that the apparent location of the variable speaker was to the right of an imaginary reference point or target azimuth" at 45 in the left field If he thought that the azimuth of the 600 Hz tone was greater than 45 he would respond left" etc Before actual testing commenced the variable speaker was set to the same azimuth as the fixed speaker and the subject was permitted to listen to the alternating sounds as long as he wished in order to establish the target" azimuth for the variable speaker During each experimental run the azimuth of the variable speaker was randomly varied in steps of 5 Testing proceeded until azimuths were identified that the subject consistently judged (3 consecutive trials) as either right or left of the target azimuth or until all azimuths in the variable field had been presented The former procedure could be employed with C, but the latter was necessary with E.

Fig. 27 presents data for fixed azimuths of 0 and 15 45 and 75 in each auditory field The datum point at each azimuth is the percentage of trials on which each subject correctly responded right when the variable speaker was to the right of the target azimuth, and left when the variable speaker was to the left f the target azimuth Judgements for signals presented at plus or minus 5 from the target azimuth however were excluded from th analysis

As seen in Fig 27 subject C scored 100% correct when the fixed loud

V CRITICAL ON TIME

The curious manner in which the apparent location of the sound moved from E's left to right ear in the intracranial localization experiment suggested a critical relation between loudness and duration on the right ear Efforts to pursue this possible relationship by loudness balance technique were unsuccessful Reliable data could not be obtained. E commented that the signals did not sound the same in the two ears, but he was unable to qualify this dissimilarity further All efforts to obtain reliable points of balance between the two ears failed

We reasoned, however that the presence of such a critical relationship should be manifest in the threshold-duration function. We set out, therefore to study the relationship between threshold SPL and signal duration Thresholds were measured by the method of adjustment The subject listened to a train of tone bursts and adjusted a 2-dB step attenuator to the lowest level at which he could just hear the signal train. Off time between successive signals was held constant at 2000 msec. On-time was varied over the range from 20 to 1000 msec. The rise-decay time for each signal was 5 msec.

Fig. 29 shows results for both subjects at 500 1000 2000 and 4000 Hz. For subject C on-duration had little effect on the threshold SPL. In marked contrast, however subject E's threshold-duration functions were clearly related to signal duration. The effect was slight but apparent on the left ear and quite marked on the right ear At 500 Hz, for example threshold SPL increased more than 60 dB as signal duration was decreased from 1000 to 20 msec. Similar effects were noted at 1000 and 2000 Hz. At 4000 Hz both ears clearly demonstrated the phenomenon, but the effect was still greater in the right ear

We believe that the data shown in Fig. 29 help to explain a number of the aberrant phenomena observed in E's performance The fact that threshold is so critically dependent on signal duration, especially in E's right ear helps to explain the discrepancy between conventional manual and Békésy thresholds on this ear (see Fig. 6) For conventional manual audiometry signal duration was probably well in excess of 1000 msec. For Békésy audiometry however signal duration was only 200 msec. There may have been, in addition, an interaction between the relatively short on-time and the equally short off-time in the Békésy signal, a possibility which was not explored in the present investigation.

It is of further interest to note in Fig. 29, that E's threshold SPLs for the 1000 msec duration are considerably lower than the threshold SPLs

We found an absolute error of approximately 1 to the left for all responses Apparently E could judge position in visual space as accurately as C.

Summary

On tasks involving both absolute and relative sound localization subject E showed marked impairment Errors were both large and unreliable from trial to trial Pure tone click and sawtooth noise signals all reflected the deficit In the case of absolute localization there was a tendency for both directional and non-directional errors to be greater in the right auditory field but on relative localization little asymmetry could be discerned

Of particular significance was the patient s report confirmed by studies of intracranial localization, that for signal durations greater than 100 msec the apparent location of the sound moved over a rather wide arc generally from left to right between signal onset and termination

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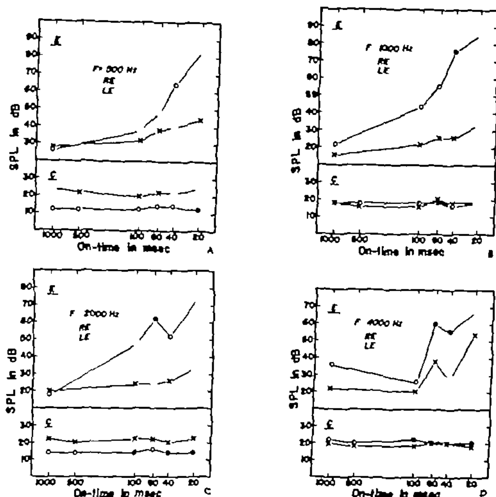


Fig. 29. Threshold SPL as a function of signal duration: (A) 500 Hz, (B) 1000 Hz, (C) 2000 Hz, (D) 4000 Hz.

obtained by conventional manual audiometry. The discrepancy is especially large at 4000 Hz where the conventional audiometric threshold SPL was more than 90 dB (Fig. 5) while the threshold SPL obtained by the method of adjustment (Fig. 29 D) at 1000 msec was only 36 dB SPL. An even lower threshold SPL was obtained at the 100 msec duration.

At first glance these discrepancies would appear to indicate nothing more than extreme instability of E's auditory thresholds. We have been impressed, however, by the fact that as this experiment progressed, E's apparently extreme instability became ever more susceptible of rational explanation. In the case of thresholds, results were critically affected by very small changes in signal parameters, but as these parameters were more rigidly specified quite repeatable results could be obtained.

A further case in point relates to sound localization. Initial results obtained for both absolute and relative localization seemed little short of chaotic. Results were superficially quite unreliable. A source at the same azimuth might be variously localized almost anywhere in auditory space

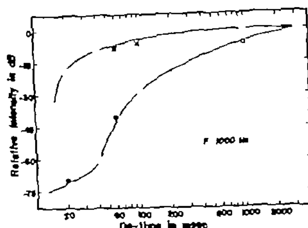


Fig. 30. Hypothetical relative intensity growth functions for E's two ears, based on the threshold data of Fig. 29 B.

on repeated trials. At times E's responses seemed little more than chance guesses. The data of Fig. 29 suggest, however, a rational explanation for this confusion. We may reason from these duration functions that the relative intensity of supra-threshold signals is also critically affected by signal duration. Fig. 30 illustrates how relative intensity might be expected to change as a function of duration in E's two ears. The data are taken from Fig. 29 B (1000 Hz) and are replotted as intensities relative to the level of the signal on the left ear at a duration of 1000 msec. Differences in threshold SPL as a function of duration are assumed to reflect differences in relative intensity of a suprathreshold signal as a function of on-time. If this transposition is valid we can see that a sound source anywhere in E's auditory space must necessarily produce a much larger initial effect on his left ear than on his right ear. The effect is so large (more than 50 dB at 20 msec) that it will effectively overcome subtle differences in phase, interaural intensity, or arrival time. Thus any sound, at any position, must, at its onset, be referred to the left ear. As the sound continues, however, the right ear makes an ever increasing contribution, and the sound image moves from left to right. After the sound has been on for about one second, the right ear is contributing almost as much as the left and the sound has moved as far to the right as it can go.

If under these circumstances, the subject is placed in a relatively unstructured situation in which a sound is presented for 10 sec, and he is instructed to report where he hears it, confusion and unreliability are quite understandable. At times he may report the apparent location at its onset, at times at its termination, at times in the middle of its duration. At other times the movement may be *so confusing that* no stable location can be assigned to it.

When the experimental task was more rigidly structured, however, as in

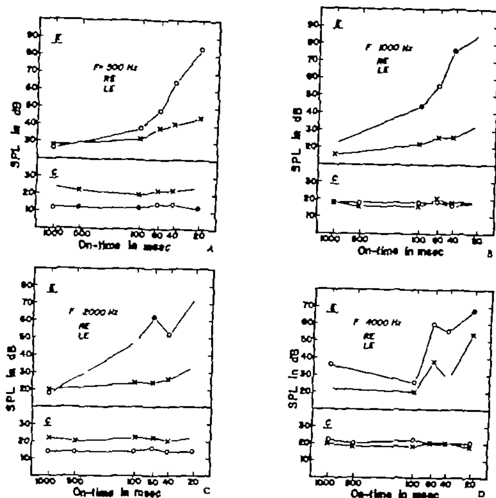


Fig. 29 Threshold SPL as a functi n of signal duration: (A) 500 Hz, (B) 1000 Hz, (C) 2000 Hz, (D) 4000 Hz.

obtained by conventional manual audiometry The discrepancy is especially large at 4000 Hz where the conventional audiometric threshold SPL was more than 90 dB (Fig. 5) while the threshold SPL obtained by the method of adjustment (Fig. 29 D) at 1000 msec was only 30 dB SPL. An even lower threshold SPL was obtained at the 100 msec duration

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VI AVERAGED ELECTROENCEPHALIC RESPONSE

The averaged electroencephalic response (AER) to auditory signals was studied by standard computer technique EEG electrodes were affixed to the scalp at the vertex and at either the right or the left mastoid process Electrodes fed an FM telemetry transmitter attached to the subject s back. The telemetered EEG was received by an FM tuner demodulated, ampli fied, and fed to an averaging computer (Mnemotron CAT 1000) The band pass of the EEG signal was 0.2 Hz to 12 Hz.

Auditory signals were delivered monaurally via earphone (Telephonic, TDH-39) at 60 dB SPL. Both pure-tone and click signals were employed. Tone bursts of 1000 Hz had durations of 200 msec, and rise-decay times of 25 msec. Click duration was 1 msec. For both tone bursts and clicks, the interval between successive signals was 2 sec. The computer sampled EEG activity over a 512 msec period following signal onset. One hundred sam ples were averaged to define each AER Each ear was tested under two con ditions of electrode placement, either vertex right mastoid, or vertex left mastoid.

Fig. 31 shows results for 1000 Hz tones. Subject C showed well-defined AER s under all four experimental conditions. Latencies of the three prin cipal deflections N P and N were 100 170 and 275 msec respectively Subject E, however failed to show clearly-defined AER s under any test conditions. Similar results were obtained at 500 Hz. Subject C showed well-defined responses, but subject E showed none. Under questioning E re-ported hearing the pure-tone signals on both ears. In addition, when asked to push a response button every time he heard a tone, E scored 100% on both ears. Yet electroencephalic responses could not be demonstrated.

Fig. 32 sh ws results f r clicks. Again C showed well-defined AER s but E howed very little response. On E's left ear there was a small but con sistent positive deflection at a latency of approximately 125–150 msec. On the right ear however there was no discernable pattern.

For control purposes AER s were obtained in response to flashes of bright light (General Radio, Strobostave) Responses to 50 successive flashe were a eraged. Fig. 33 shows the results Both C and E gave clearly d fined AER s. E' responses were, in fact, somewhat better defined than C's.

In further expl ration with E, signal intensity signal frequency repe-tition rate and computer sampling period were all varied in an effort to

the intracranial localization experiment E's responses, while still somewhat confused, became much more understandable. By and large signals presented in phase and at equal intensity to the two ears tended to be heard first in the left ear then to move toward the right ear.

In effect, the critical duration phenomenon renders any localization data ambiguous. E's judgements of apparent localization based on 10 sec signals are confounded by the on time effect to an unknown degree.

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Auditory signals were delivered monaurally via earphone (Telephonic, TDH-39) at 80 dB SPL. Both pure-tone and click signals were employed. Tone bursts of 1000 Hz had durations of 200 msec, and rise-decay times of 25 msec. Click duration was 1 msec. For both tone bursts and clicks, the interval between successive signals was 2 sec The computer sampled EEG activity over a 512 msec period following signal onset. One hundred samples were averaged to define each AER. Each ear was tested under two conditions of electrode placement, either vertex-right mastoid, or vertex left ma toid

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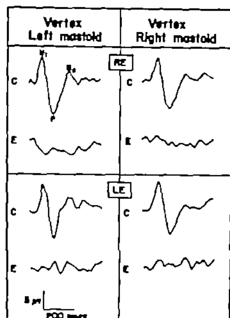


Fig 31

Fig 31 Computer averaged electroencephalic responses (AER) t 100 successive tone bursts. The frequency was 1000 Hz nd the interval between tones was 2 sec

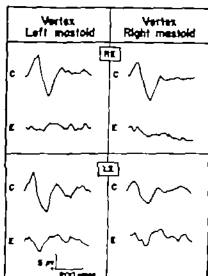


Fig. 32.

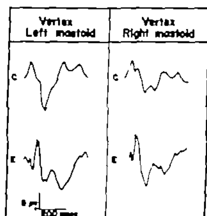


Fig. 33.

Fig 32 Comp t r averaged lectroencephalic responses (AER) to 100 ccessive click at 2 sec intervals.

Fig 33 Comput r averaged electroencephalic responses (AER) to 50 fl she f light t 2 sec int rvals.

find some combination of parameters that might elicit an AER All efforts were fruitless It should be noted however that we did not explore the early" response in the range from 0–60 msec (Goldstein and Rodman, 1967)

In any event the failure to obtain "slow" responses (Davis and Zerlin, 1966) in the 0–500 msec range is of some interest. We have here a situation in which the patient "hears" the sounds, attends closely by pushing a button every time he "hears" the sound, and yet fails to demonstrate an AER in response to sound.

VII DISCUSSION

Little difficulty is encountered in anatomic localization of the lesions in this case. Although the patient had mixed dominance, the initial presentation with aphasia, right sided sensory symptoms and right facial paresis indicated a left cerebral hemisphere lesion. This conclusion was confirmed by the EEG, brain scan and arteriographic studies. The second phase of the illness, although not associated with further clinically localizing or lateralizing phenomena, was clearly related to a right cerebral hemisphere lesion, again on the basis of EEG, brain scan, and arteriographic data. It is our contention that these bilaterally placed cerebral lesions were directly responsible for the patient's hearing loss. The audiological data presented support this thesis. Nonetheless, the mere coincidental existence of cerebral lesions and hearing loss does not in itself prove causality, exclusion of other possible responsible sites being essential for the establishment of such a relationship.

The tuning fork tests and bone conduction audiograms proved the hearing loss to be of the sensori-neural type. The data obtained from speech audiometry further narrowed the range of anatomic considerations by pointing away from cochlear disease. In order to establish a causal relationship between the cerebral lesions and the hearing loss, only the further possibilities of auditory nerve and brainstem disease need to be excluded. The abrupt onset of bilateral hearing loss, the absence of vertigo and tinnitus, the lack of exposure to ototoxic agents and acoustic trauma, the normal CSF, the negative skull X-rays and the normal caloric responses to ice water, though certainly not diagnostic when taken each in isolation, at least make significant auditory nerve disease highly improbable when considered in toto. This is particularly true in view of the marked disturbance of auditory nerve function which would be required to produce the striking severity of loss exhibited by this patient at the time of his second admission. Since the brainstem contains a closely packed mass of neural elements, which, in addition to audition, are intimately concerned with motor, sensory, oculomotor, vestibular, postural, bulbar, reflex and autonomic functions, one would certainly expect disturbances in at least some of these functions, were the patient's deafness to be caused by disruption of the brainstem auditory pathways. This concept is illustrated by the five patients with brainstem disease and audiologic abnormalities reported by Fichel, Hedgecock and Williams (1960). All of those patients had rather striking symptoms or signs specifically referable to the brainstem. Such was not the case with our patient. The minor abnormalities found in motor

sensory and reflex functions were, as has been pointed out, referable to cerebral hemisphere disease. Thus, a brainstem cause of hearing loss is also extremely improbable

The patient s clinical course was characteristic of cerebral infarction as were the evolutionary changes seen on EEG (Kiloh and Osselton, 1961) and brain scan (Rhoton, Kinkerfuss, Lilly and Ter-Pagossian, 1966 Molinari, Pircher and Heyman, 1967) The arteriographic demonstration of bilateral occlusions of the distal middle cerebral branches gave graphic evidence of the lesions responsible for such infarction. However the etiology remains obscure The patient had a wide pulse pressure with systolic hypertension, probably due to thyrotoxicosis rather than to one of the hy pertensive vascular diseases. Detailed anamnestic, physical and laboratory investigation failed to disclose any evidence of diabetes mellitus, syphilis, migraine a hypercoagulable state, cardiac disease, inflammatory angiopathy blood dyscrasia, congenital aneurysm or other vascular anomalies. Indeed, the only laboratory abnormalities detected, outside of those directly related to thyroid function, were some minor non-specific changes in serum protein electrophoresis and immunoglobulin patterns and a small elevation in serum viscosity The latter is frequently found following cerebral in farction and is also, therefore not of diagnostic aid in this case (Eisenberg, 1960) Thus, none of these findings resulted in an etiologic diagnosis. To our knowledge, thyrotoxicosis cannot be directly implicated as a cause f cerebrovascular occlusion except when it is associated with cardiac arrhythmia, mural thrombus formation and embolization. Although no evi dence of atrial fibrillation was obtained through five months of in hospital evaluation, including radial pulse counting four times daily and during sleep during three of these m nths, this possibility cannot be entirely dismissed from consideration but appears remote The occurrence of occlusive cerebrovascular disease in young adults is not an uncommon phenomenon (Berlin, Tumarkin and Martin, 1955 Louis and McDowell, 1967) Middle cerebral artery occlusion particularly is common in the younger age group among the 59 cases reviewed by Lascelles and Burrows (1965) 29 were less than 50 years old, and 10 were less than 30 years old. At the present time then, no etiologic diagnosis is possible in our patient.

We conclude from these data that the patient whose case is here presented experienced, at two different points in time, occlusion of the ter minal branches f the middle cerebral artery on each side, resulting in bilateral partial cerebral hemisphere infarction, maximal in the temporal lobes, and producing the clinical picture of cortical deafness.

The evaluation of audit ry function in the present patient revealed a complex configuration of assets and deficits. Although auditory sensitivity a measured by conventional manual audiometry was grossly unimpaired, t nal "threshold particularly on the patient s right ear were critically dependent on pecifiable signal parameters, especially on-duration This factor appeared to underlie both threshold instability and impaired sound

localization Its rigid control in the further study of patients with temporal lobe lesions, is urgently *recommended*

In spite of the bilateral configuration of this patient s lesions, performance on tasks involving speech intelligibility and loudness discrimination was measurably poorer on the right ear This result is consistent with previous demonstrations (Bocca *et al.*, 1955 Bocca 1958 Jerger 1960 B Jerger 1964) that elementary auditory perceptual tasks reflect the lateralization of temporal lobe damage rather than impairment in the hemisphere dominant for speech Left temporal lobe damage produces poorer performance on the right ear and right temporal lobe damage produces poorer performance on the left ear Indeed the very fact of ear differences argues that these simple tasks probe aspects of auditory perception with dual representation in the two hemispheres They must in effect tap performance at a level well below the language function of the dominant hemisphere In the present patient these ear differences merely suggest greater damage to the auditory areas of the left temporal lobe.

Surprisingly however performance on tasks involving temporal ordering of auditory events failed to show these ear differences Both ears reflected about the same degree of impairment

This set of findings is consistent with Efron s (1963) argument that temporal analysis is performed in the dominant temporal lobe According to Efron s hypothesis the temporal analysis of sequence is a relatively *high level perceptual function and is localized in the hemisphere dominant* for speech On the basis of this argument it is entirely predictable that our patient should show equivalent impairment in temporal ordering no matter which ear is tested

If temporal ordering were at the same perceptual level as the speech intelligibility and loudness discrimination tasks, then we should have expected to find the same ear differences on temporal order as on the speech and loudness tasks. On the contrary the experimental findings for temporal order showed no ear differences, a result consistent with the hypothesis that the perception of temporal sequence is, indeed, a function of the dominant hemisphere

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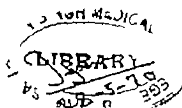
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SUPPLEMENTUM 257

Central Institute for the Deaf St. Louis, Missouri

DEVELOPMENT OF SPEECH SOUNDS IN CHILDREN[1]

S EGUCHI and L J HIRSH

UPPSALA 1969

CONTENTS

[1] *This research was supported in full by U.S. Public Health Service Department of Health, Education and Welfare research grant (NB-03856) from the National Institute of Neurological Diseases and Blindness.*
Visiting Research Associate at C.I.D., on leave from Dept. of Otolaryngology, University of Nagasaki

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I INTRODUCTION

Reviews of the literature concerned with development of speech in children have provided much information on grammatical, contextual and syntactic aspects (Miller and Smith, 1966) but somewhat less on phonetic aspects (Irwin, 1943, 194 1948 Morley 1965 Simon, 1957) of speech development Phonetic studies, particularly since the introduction of the Sound Spectrograph in 1946, have clarified certain acoustical chracteristics of speech sound (Potter Kopp and Green, 1947 Joos, 1948 Peterson and Barney 1952 Potter and Steinberg, 1950 Peterson, 1950) and these characteristics have been confirmed subsequently by acoustical resonance theory (Dunn, 1950 Stevens and House 1955, 1961 Fant, 1960 Cooper *et al* 19 2) Potter and Steinberg (1950) and Peterson and Barney (1952) reported that the vowel formant frequencies of children were about 25% higher than those of the adult male and 20% higher than those of the adult fem le The rapid anatomical, physiological and psychological development in childhood would, of course predict that these acoustical features of the speech sounds or phonemes of children could not remain stable over any long period of time However there is a scarcity of acoustical studies con cerned with the development of speech sounds or phonemes in children (Okamura, 1966)

The present investigation was designed to clarify the way in which speech sounds or phonemes develop in normal children after the initial stages of language acqui ition. Measurement of the formant frequencies that charac terize certain vowels in a sentence spoken by children at different ages would provide information on the formant shifts that occur with age Furthermore calculation of the variability of such formants in samples of repetitions of the sentences would provide information on the accuracy with which children uttered such vowels. Measurement of the vocal fundamental frequency would provide information on changes with age and another kind f measurement namely of certain interphonemic time intervals, would pr vide b th mean and variability f r at least one aspect of consonant devel opment Finally to ascertain what relation might exist between variability of vow l formant and the intelligibility of vowels, certain listening tests were carried out

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II GENERAL PROCEDURE

Subjects

Eighty four subjects, ranging in age from 3 to 13 years, and also adults, served as talkers Subjects older than 10 years were divided into two groups according to sex Each age or age-sex group contained five or six subjects. All subjects were from the Greater St Louis area

Test material

Two sentences, He has a blue pen" and "I am tall" which are easy to pronounce and available in the daily conversation of children were selected as the test sentences.

Six vowels, representative of a variety of tongue positions in vowel arti culation were selected for spectrographic analysis, in order from the sen tences above [i] [æ] [u] [ɛ] [a], [ɔ] (The sound of [a] not normally found in most American dialects, was taken from the first portion of the diphthong [ai] in the word I) In addition the words "blue "pen" and tall were used for the measurement of certain temporal features in the words.

Recording procedures

Tape recordings of the test sentences were made in a room where the signal to-ambient noise ratio was 32 dB or better Each sentence was spoken by each subject on five different occasions, separated by only a few minutes. Children over 7 years of age read the sentences from a card, while younger subjects repeated them after a native American speaker (IJH) who speaks with a general Eastern dialect Speech samples at approximately 70 dB SL (re 0 0002 dyne/cm^2) were picked up by a condenser microphone at a distance of about 0.5 meter and were recorded on tape by an Ampex (Model 300) tape recorder Background and internal noise was further reduced by a 300-Hz high pass filter whose low frequency response fell at 12 dB per octave

III VOWEL FORMANT FREQUENCIES

Method

A Sound Spectrum Analyzer (Kay Sona-Graph Model 6061A) was used for the acoustical analysis of reproduced speech sounds. Steady-state por tions f the vowels were identified from both wide-band and narrow band pectrograms. The first and second formant frequencies for each vowel on each repetition of each subject were estimated from the spectrum envelopes drawn on expanded narrow-band sections (0–4000 Hz) (Fig 1)

In each age group, the mean formant frequencies and between subject standard deviations were calculated from the mean values of each subject, while intra-subject standard deviations were calculated as the square root of the mean value of the individual variance within each age group

These intra-subject standard deviations of the distribution of five repeti tions within each age group were used as a measure of variability or the inverse of precision, of articulation and were calculated either in absolute term or in terms of ratios to the individual means.

Since the present study focuses on measures of variability associated with talker repetitions, age and different vowels, some information about error of measurement of formant frequencies through visual inspection of spectrogram sections is required Several previous reports have addressed them selves to this problem. With age as a principal variable Potter and Stein berg (1050) reported no correlation between the fundamental frequency and f rmant frequency for their three groups of adult males, adult females, and children More directly related to the present report was their further find ing that repeated utterances by a number of talkers showed a standard deviation of 20–40 Hz f r the first f rmant, and 40–70 Hz for the second formant Corresponding measurements for children (8 years) yielded values about twice a larg Distributions of ingle utterances from a large number of talkers had standard deviations two or three times as large Peterson and Barney (1052) reported that the standard deviation for the first formant of a repeated vow l ([i]) by adult females was 15.3 Hz. They did not attribute thi value to a specific source but uggested that it represented intra subject riability that is, over several trials by the same talker and they stated further that this value was not easily interpretable in comparing one talker with another Finally and more specifically concerned with error of spectrographic me urement, Lindblom (1962) studied the accuracy with which formant frequencies could be estimated from spectrograms of synthesized vowels. He compared the values read by five experienced investigators and bt ined a between-reader standard deviation of 40 Hz for adult male voice pitch, that is, a alue about one-f urth the fundamental frequency

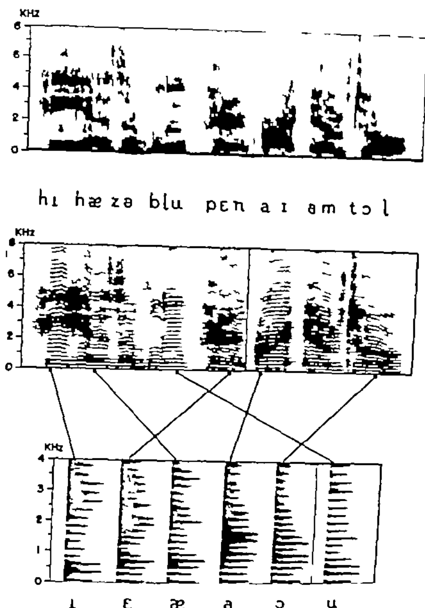


Fig 1 Spectrogram of a child' rendition of "H ha blue pen I am t ll Wide-band spectrogram is shown at the t p, and narrow band i the center At the bott m re seen the section t th indicated points in time which show the spectral dist ibuti f th vow is up to 4 kHz

We cannot find any study on intra reader variability that is, the relia bility with which a single investigator will draw his spectrum envelopes and interpolate the peak values on successive readings of the same recorded sample Accordingly one of us (S E.) estimated from sections the first and second formants of six different vowels spoken by a 6-year-old child and by an adult male Five sets of narrow-band sections (0–4 kHz) were recorded from the spectrogram and he then made his estimates on different occasions and in haphazard order The typical standard deviation within any set of five was about 10 Hz, a value considerably lower than any that will

TABLE 1a–f *First and second formant frequencies for six vowels*

1 each age or sex-age sub-group N = 5. Each table section concerns one vowel, and within each section the columns represent, in order the Mean frequency the Between-subject standard deviation, the Within-subject standard deviation, and the Ratio of the Within-s.d. t the Mean.

Age (yrs.)	Mean	Bet een-S s.	Intra-S s.D	Ratio of Intra-S s. to Mean
a. ?				
First formant				
3	481	81.2	53 1	110
4	441	49.5	41.6	093
5	408	63.3	37.0	091
6	397	15.2	30.3	076
7	411	19.6	28.6	070
8	397	38.1	23.6	060
9	400	38.9	21 4	053
10	403	38 9	19 4	.048
11 M	397	17.0	18.5	.047
11 F	423	81.3	18.1	.043
12, M	359	62.1	17 6	049
12, F	358	33.5	17.3	048
13, M	353	51 6	16.0	045
13, F	377	30.2	16.2	.043
Adult M	288	31.3	15.2	.053
Adult, F	338	21 1	14.9	.044
Second formant				
3	3318	267 1	130.8	039
4	3030	453.1	101.0	034
5	3235	348 3	93.8	.030
6	3105	218.3	89 6	.025
	3301	187 1	78.8	.021
8	3101	67.9	71 1	023
9	3106	171 5	58.7	019
1	3025	167 7	56.5	019
11 M	2778	98.7	46.5	017
11 F	3131	179.2	46 1	015
12, M	2577	49.8	39.6	.014
12, F	2910	183.7	40.3	.014
13, M	2727	279 7	31.9	.013
13, F	2907	276.2	41.0	014
Adult M	221	191 4	33.5	015
Adult, F	2310	72.5	39 4	.014
b.				
First formant				
3	672	77 1	97.8	145
4	606	84 0	78.7	139
5	612	61 1	65.4	103
6	72	61 1	55 3	108

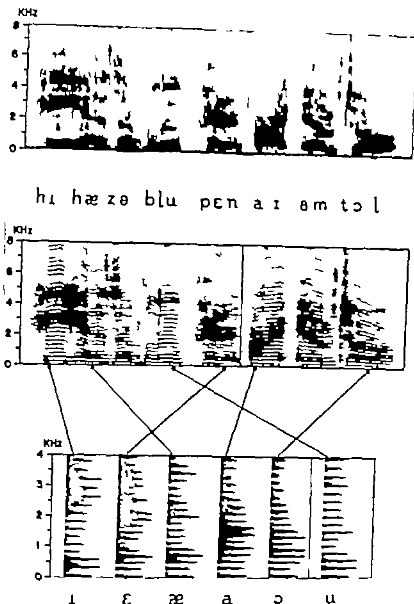


Fig. 1. Spectrogram of a child's rendition of "He has a blue pen. I am tall." Wide-band spectrogram is shown at the top and narrow-band in the center. At the bottom are seen the sections at the indicated points in time which show the spectral distribution of the vowels up to 4 kHz.

We cannot find any study on intra-reader variability, that is, the reliability with which a single investigator will draw his spectrum envelopes and interpolate the peak values on successive readings of the same recorded sample. Accordingly, one of us (S. E.) estimated from sections the first and second formants of six different vowels spoken by a 6-year-old child and by an adult male. Five sets of narrow-band sections (0–4 kHz) were recorded from the spectrogram and he then made his estimates on different occasions and in haphazard order. The typical standard deviation within any set of five was about 10 Hz, a value considerably lower than any that will

TABLE 1a–f *First and second formant frequencies for six vowels.*

For each age or sex-age sub-group N = 5. Each table section concerns one vowel, and within each section the columns represent, in order the Mean frequency the Between-subject standard deviation, the Within-subject standard deviation, and the Ratio of the Within-s.d. to the Mean.

Age (yrs)	Mean	Between-S s.d.	Intra-S s.d.	Ratio of Intra-S s.d. to Mean
a. /i/				
First formant				
3	481	81.2	53.1	110
4	444	49.5	41.5	093
5	408	63.3	37.0	091
6	397	15.2	30.3	.076
7	411	19.5	28.6	.070
8	397	34.1	23.8	.060
9	403	54.9	21.4	.053
10	403	36.9	19.4	.048
11, M	397	17.0	18.5	.04
11, F	423	81.3	18.1	043
12, M	230	82.1	17.6	019
12, F	258	33.5	17.3	018
13, M	353	54.8	16.0	015
13, F	377	30.2	16.2	013
Adult, M	288	31.2	15.2	.053
Adult, F	325	21.1	11.9	.044
Second formant				
3	3318	287.1	131.8	.039
4	3030	443.1	101.0	031
5	3233	316.3	93.6	030
6	3106	210.3	89.4	029
7	3201	187.1	6.9	.021
8	3101	87.9	71.1	.023
9	3106	171.5	58.7	019
10	3023	167.7	56.5	019
11, M	2778	98.7	46.5	017
11, F	3131	179.2	48.1	015
12, M	2577	49.0	39.5	014
12, F	2940	183.7	40.2	.014
13, M	2727	270.7	31.9	013
13, F	2907	294.3	41.0	014
Adult, M	2217	191.4	33.6	015
Adult, F	2519	72.5	39.4	.014
b.				
First formant				
3	673	77.1	97.8	143
4	566	68.0	78.7	139
5	612	81.4	64.1	13?
	612	81.5	55.3	109

Table 1 (*continued*)

Age (yrs.)	Mean	Between S s.D	Intra-S s.D.	Ratio of Intra-S s.D to Mean
7	681	131.5	50...	0 6
8	583	77 1	15.5	078
9	608	119	10.3	066
10	645	106.9	33 2	051
11 M	671	15.2	27 7	041
11 F	628	171.2	30.0	048
12, M	618	82.3	25.3	041
12, F	687	51.5	1.8	036
13 M	668	62.5	21.2	032
13 F	590	141 8	22.1	037
Adult M	555	91 7	21 0	038
Adult F	589	106.5	1 6	037
Second formant				
3	2083	180 6	111	031
4	2397	205 0	119 6	050
5	2118	157 8	96.5	040
6	2281	198.3	92.0	041
7	2280	101.5	73.1	032
8	2193	142.2	69 8	032
9	2290	158 1	69.5	030
10	2193	163.3	59.5	027
11 M	2109	73 1	51 4	024
11 F	2359	187 6	51 5	022
12 M	2059	123 9	48.2	023
12, F	2169	104.3	44.5	021
13 M	19 4	198.1	41 8	021
13 F	2205	226.3	46.0	021
Adult M	1726	0 5	38.5	022
Adult F	2111	101.5	45	021
e /æ/				
First formant				
3	786	107 9	102.2	130
4	637	121 3	86.5	132
5	643	90 4	68.8	107
6	611	98 5	58.8	096
	730	113 1	56.1	0 6
8	685	77 3	51 1	073
9	617	53 7	47 0	073
10	735	17.5	37.3	051
11 M	670	88 9	34 1	055
11 F	736	141 4	34 6	04
12, M	638	48 5	33.9	032
1 F	700	39 8	33 5	048
13 M	658	0 1	29 5	045
13 F	672	50 3	29 1	044
Adult M	616	68.6	25 1	041
Adult F	61	5 7	30.3	040

Table 1 (*continued*)

Age (yrs.)	Mean	Between-S s.d.	Intra-S s.d.	Ratio of Intra-S s.d. to Mean
Second formant				
3	2390	203.4	131.6	.032
4	2281	213.4	112.3	.049
5	2423	201.9	101.1	.042
6	2238	144.1	93.9	.042
7	2299	137.2	86.2	.037
8	2222	101.3	83.9	.030
9	2293	102.3	76.3	.033
10	2235	110.6	70.6	.031
11, M	2063	123.3	68.1	.033
11, F	2246	100.1	61.2	.028
12, M	2012	101.5	63.3	.031
12, F	2136	113.2	60.3	.028
13, M	1883	225.7	56.9	.030
13, F	2181	214.9	57.1	.026
Adult, M	1723	63.3	59.5	.036
Adult, F	2051	83.5	61.5	.030

4. /

Age (yrs.)	Mean	Between-S s.d.	Intra-S s.d.	Ratio of Intra-S s.d. to Mean
First formant				
3	986	103.9	168.9	.171
4	879	146.7	121.5	.138
5	1037	227.9	110.2	.106
6	809	103.1	87.2	.108
7	940	81.4	74.0	.078
8	921	90.8	69.2	.073
9	1033	109.4	63.5	.060
10	997	131.9	51.8	.033
11, M	881	37.5	39.5	.013
11, F	1005	149.7	47.2	.047
12, M	913	110.5	38.7	.012
12, F	893	58.5	37.5	.012
13, M	900	121.1	31.3	.039
13, F	930	51.0	36.0	.038
Adult, M	813	100.7	31.8	.043
Adult, F	922	83.9	37.4	.041
Second formant				
3	1992	180.8	154.2	.079
4	1858	211.8	137.5	.074
5	1761	114.2	119.6	.067
6	1833	83.3	95.5	.060
7	1642	119.6	83.2	.050
8	1729	133.7	77.1	.013
9	1685	87.2	73.7	.011
10	1709	127.3	86.9	.030
11, M	1538	136.8	53.9	.033
11, F	1732	52.9	53.8	.032

Table 1 (*continued*)

Age (yrs.)	Mean	Between-S S.D	Intra-S S.D	Ratio of Intra-S S.D to Mean
7	661	131 5	50.2	0 6
8	585	7" 1	45 5	0"8
9	608	119.2	10.3	066
10	645	106 9	33.2	031
11 M	671	13.2	27 7	041
11 F	628	171 2	30 0	018
1_, M	618	82.3	23.3	041
12, F	637	51.5	21 8	036
13, M	668	62.5	21 2	032
13 F	590	141 8	22 1	037
Adult M	553	91 7	21 0	038
Adult F	589	106.5	21 6	037
Second formant				
3	"683	180 6	141 7	031
4	2397	203.0	119 6	050
5	118	157 8	90.5	010
6	"281	198.3	92.9	041
7	2280	101.5	"3.1	032
8	193	142.2	69 8	032
9	2296	158.1	69 3	030
10	2193	163.3	50 5	027
11 M	2109	"3 1	51 1	021
11 F	339	187 6	51.5	0"2
12, M	"039	123.9	48.2	023
12 F	169	101.3	41.5	021
13 M	1974	196 1	41 8	021
13 I	2203	226.3	16.0	021
Adult M	1"20	0 5	38.5	022
Adult F	2111	101 5	15.2	021
e /æ/				
First formant				
3	786	107 0	102.2	130
4	657	121 3	86.5	132
5	643	90 4	68 8	107
6	611	98.5	58 8	096
7	"36	113 1	50.1	0 6
8	685	77.3	51 1	075
9	647	53.7	17 0	073
10	"35	47 5	37.3	051
11 M	620	88 0	31 1	053
11 F	"30	141 4	31 6	017
12, M	658	48.5	33 9	052
1_, F	700	39 8	33.5	018
13 M	658	"0 1	29 5	015
13, F	672	86.5	29 1	011
Adult M	616	68.6	25.1	011
Adult, F	61	"5.7	30.3	010

Table 1 (continued)

Age (yrs.)	Mean	Between-S s.d.	Intra-S s.d.	Ratio of Intra-S s.d. to Mean
5	432	41.4	30.2	.067
6	431	28.6	31.2	079
7	481	49.0	30.8	.064
8	450	63.2	24.9	.055
9	469	63.5	23.1	049
10	460	33.1	19.2	.041
11 M	418	28.8	15.9	.035
11 F	478	77.1	18.7	.039
12, M	401	47.0	16.0	.040
12, F	422	31.2	16.8	.040
13, M	425	18.8	15.4	.036
13, F	399	31.9	15.9	.040
Adult M	311	45.9	10.2	017
Adult, F	356	35.0	14.5	041
Second formant				
3	1641	209.7	120.8	.072
4	1828	149.4	97.6	061
5	1477	112.3	84.2	.058
6	1385	117.9	78.2	056
	1525	67.8	67.3	.044
8	1437	51.7	61.0	048
9	1392	115.6	61.7	044
10	1351	92.8	56.9	.042
11 M	1398	111.6	53.6	0.38
11 F	1474	91.2	49.5	.034
12, M	1253	120.4	46.7	.037
12, F	1436	61.9	47.8	.033
13, M	1317	103.9	43.1	.033
13, F	1420	203.2	46.8	0.33
Adult M	1234	80.5	43.6	.035
Adult F	1160	2.7	46.1	029

be described presently. Since this crude measure of reader error was the same for both ages or for all vowels, we conclude that the measures of variability to be described in the following sections are in fact descriptive of the speech productions.

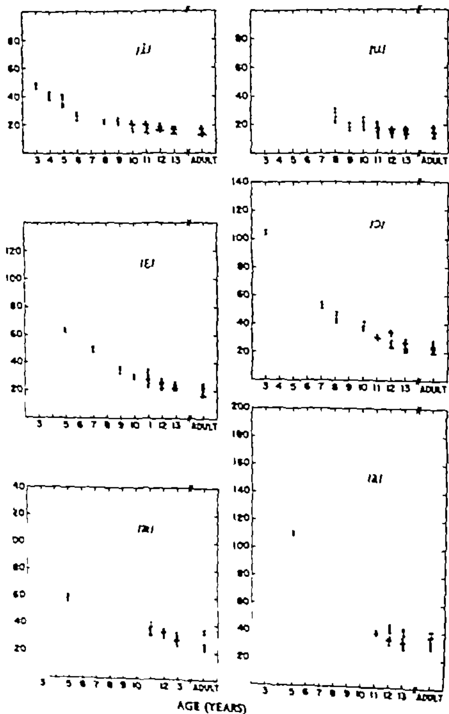
Results

Means for each age group and standard deviation between and within subjects for first-formant and second-formant frequencies are given in Table 1.

Mean values of first formant and second-formant frequencies. The second formant frequency (first column, lower half) tended to drop more than did

Table 1 (continued)

Age (yrs.)	Mean	Between S S.D.	Intra S S.D.	Ratio of Intra S S.D. to Mean
12, M	1573	101 1	50.1	032
12, F	1734	1 6 7	50.3	029
13, M	1520	00,*	16.1	030
13 F	1719	138 9	13.8	0_5
Adult M	1301	60.3	41 8	031
Adult F	1503	110 1	41	020
e /ɔ/				
First formant				
3	802	110.3	109 6	13
4	62	111 6	83.3	109
5	901	107 0	79 6	088
6	689	87 2	62.5	091
	817	78.8	53 1	063
8	743	69 7	48 1	065
9	830	68.7	45.2	031
10	814	89 6	39.2	018
11 M	724	67 6	31 5	018
11 F	799	114 1	31 8	040
12, M	703	100 5	31.2	044
12 F	830	89 5	28 1	034
13, M	744	85 7	1.5	033
13 F	806	126.1	21 6	031
Adult M	653	30.5	_3.3	036
Adult F	666	38 9	21 1	036
Second formant				
3	1185	70.8	122 1	082
4	1300	172.7	93 1	067
5	1513	109 6	80.3	053
6	1308	11 3	68 1	05
	1398	91 9	61 8	016
8	1359	78 3	63 2	04
9	1352	116.2	51 7	040
10	1336	18 0	52.0	039
11 M	1281	87 5	17 5	037
11 F	1325	101 9	41 2	033
12, M	1175	139 3	10 9	035
12, F	1382	82.5	40.1	029
13 M	1120	82.8	11 0	037
13 F	1802	155 9	42.1	035
Adult M	1013	67 1	10 6	039
Adult F	1135	95 1	41 0	03
L /u/				
First formant				
3	578	74.2	65.7	096
4	172	21 7	42.0	089



ry 3 Intra-subject riability I first formant for al vowel function of ge
ach point represent the standard deviation in Hz for each subject used I the experi
ent thus he ge of 10, females re indicated by f lled circles, while males re
ndicated by open circles.

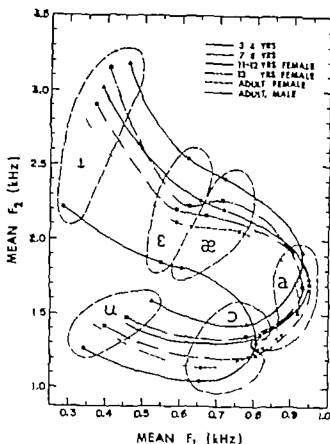


Fig. 2. Mean formant frequencies for combined age groups as shown in the key. Each point represents the combination of Formant 1 and Formant 2 for each of the six vowels. *The different symbols together with the lines that join them represent the different ages.* The broken circles are drawn round all points for a given vowel.

the first formant frequency (first column, upper half) with the exception of the first formant frequency for the vowel [a]. This was especially clear during the period from 3 to 5 years. Formant frequencies of 13-year-old girls were close to those of adult females, while 13-year old boys had higher formant frequencies than did adult males. Formant frequencies of adults showed almost the same values as those found in the literature (Peterson and Barney 1952, Fairbanks and Grubb, 1961, Potter and Steinberg 1950).

In order to assess the dependence of formant frequencies on age, values were averaged for the following age groups: 3 and 4 years, 7 and 8 years, 11 and 12 year-old girls, 13 year-old girls, and male and female adults. The *results are shown in Fig. 2 as the familiar F_1–F_2 plot* with the vowels of each age group connected to form a "vowel triangle".

Here, the gradual but marked decrease in second formant frequencies, as contrasted with the more stable first formant frequencies, is shown. Another feature that stands out is that the first formant frequency for [a] appears to be independent of age.

Between subject standard deviations. Standard deviations of the distribution of individual subject means *(second column)* within each age group

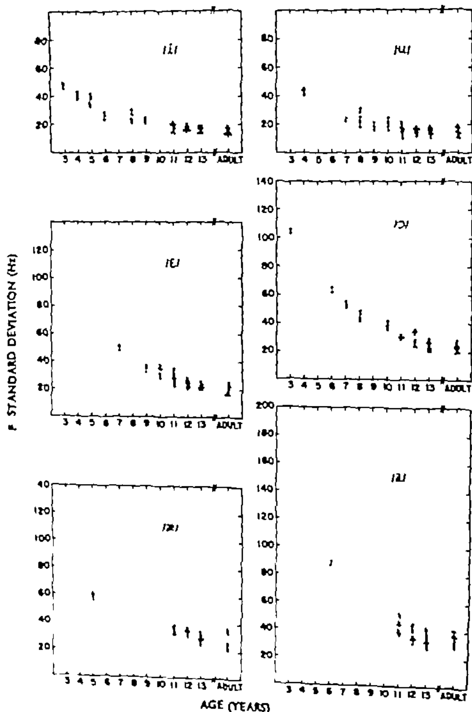


Fig. 3. Intra-subject [illegible] riability in first formant for six vowel[illegible] [illegible] function of [illegible] Each point represent[illegible] the standard deviation i[illegible] Hz for each [illegible]ubject [illegible] the experi-ment. Above the [illegible]ge of 10, females [illegible]re indicated by filled circles, whil[illegible] males [illegible]re indicat[illegible]d by open circles.

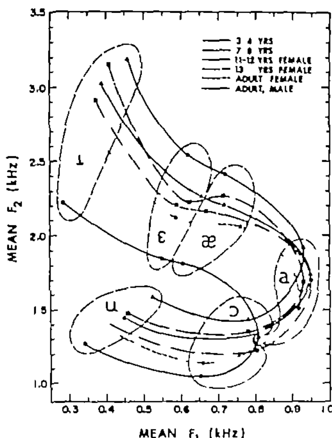


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the first formant frequency (first column upper half) with the exception of the first formant frequency for the vowel [ɑ]. This was especially clear during the period from 3 to 5 years. Formant frequencies of 13-year-old girls were close to those of adult females, while 13-year-old boys had higher formant frequencies than did adult males. Formant frequencies of adults showed almost the same values as those found in the literature (Peterson and Barney 1952, Fairbanks and Grubb, 1961, Potter and Steinberg 1950).

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Here, the gradual but marked decrease in second formant frequencies, as contrasted with the more stable first formant frequencies, is shown. Another feature that stands out is that the first formant frequency for [ɑ] appears to be independent of age.

Between subject standard deviations. Standard deviations of the distribution of individual subject means (second column) within each age group

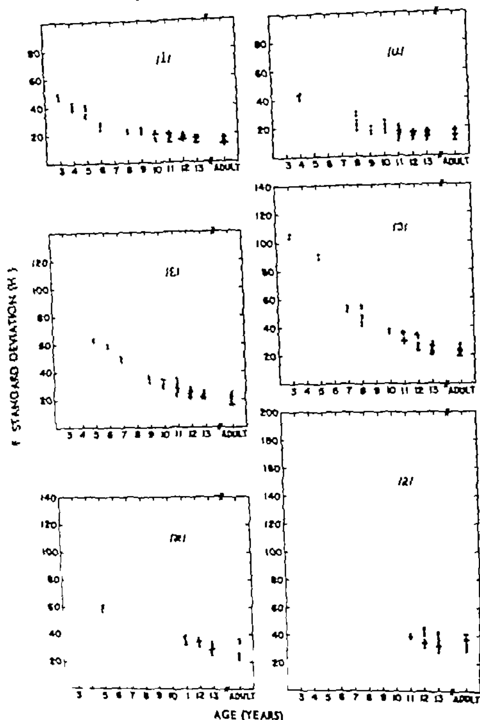


Fig. 3. Intra-subject variability in first formant for six vowels as a function of age. Each point represents the standard deviation in Hz for each subject used in the experiment. Above the age of 10, females are indicated by filled circles, while males are indicated by open circles.

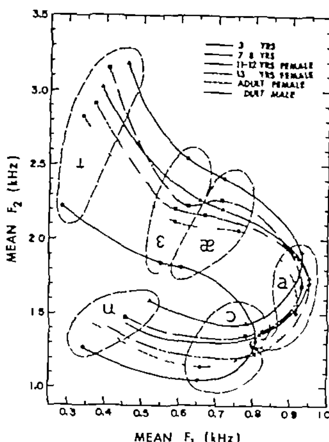


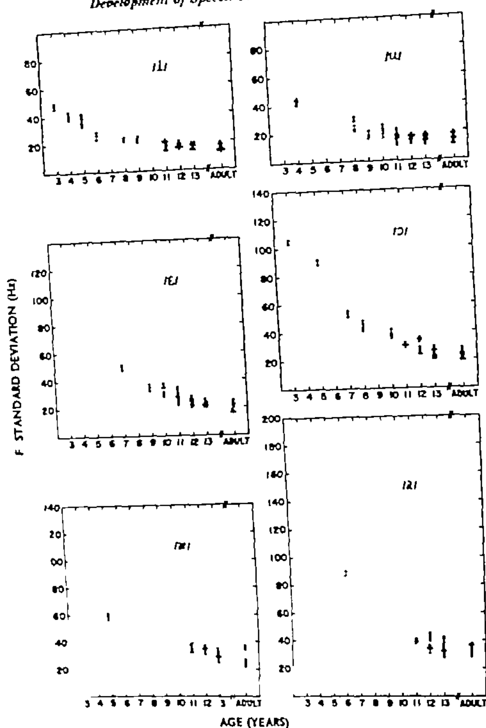
Fig. 2. Mean formant frequencies for combined age groups as shown in the key. Each point represents the combination of Formant 1 and Formant 2 for each of the six vowels. The different symbols together with the lines that join them represent the different ages. The broken circles are drawn around all points for a given vowel.

the first formant frequency (first column, upper half), with the exception of the first formant frequency for the vowel [a]. This was especially clear during the period from 3 to 5 years. Formant frequencies of 13-year-old girls were close to those of adult females, while 13-year-old boys had higher formant frequencies than did adult males. Formant frequencies of adults showed almost the same values as those found in the literature (Peterson and Barney 1952, Fairbanks and Grubb, 1961, Potter and Steinberg 1950).

In order to assess the dependence of formant frequencies on age, values were averaged for the following age groups: 3 and 4 years, 7 and 8 years, 11 and 12 year-old girls, 13 year-old girls, and male and female adults. The results are shown in Fig. 2 as the familiar F_1–F_2 plot with the vowels of each age group connected to form a "vowel triangle".

Here, the gradual but marked decrease in second formant frequencies, as contrasted with the more stable first formant frequencies, is shown. Another feature that stands out is that the first formant frequency for [a] appears to be independent of age.

Between subject standard deviations. Standard deviations of the distribution of individual subject means (second column) within each age group



F g 3 Intra subject riability in first formant for al vow l function f ge Each point represent the st nd rd deviation in Hz for each subject sed i the experiment Abov the ge of 10, females re indicated by filled circles, while males re indicated by open circles.

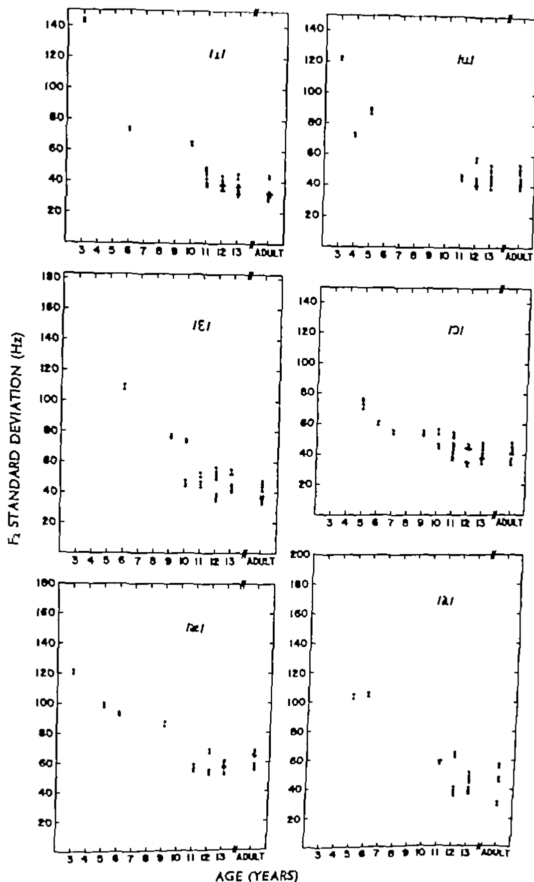


Fig 4 Intra bject vari bility f second f rm t Ea h point represent th st d rd devi ti in H f each bject used i th e perim nt Above the ge of 10, f mal re indicated by filled circles, whil males re indicated by open circl s.

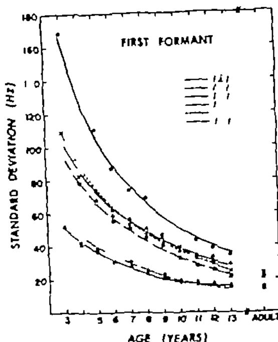


Fig 5 Intra-subject riability i Formant 1 typical f the different age groups function of ge I thi figure each point represent the square root of the erage ariance for the children i each ge group. The different ymbol nd the different lines connecting them for each f the si vowel re identified i the key

for the first and second formant frequencies varied between 40 and 450 Hz. Age does not appear t be a factor in between-subject standard deviations f r either the first or second-formant frequency In other words, individual's mean formant frequencies do not appear to become more like each other a the indi iduals get older

Intra-subject tandard deviations The five sentence repetitions permitted calculation of intra-subject standard deviation f r first and second-formant frequencies, which are shown in Figs. 3 and 4 respectively Each point represents a tandard deviation for each subject The filled points show data for female subjects bove the age of ten.

The ariability of first-formant frequ ncies was higher for middle vo l than f r high-front and high-back vowels, but f r all vowels the riability decreases with age reaching a minimum value which corre- p nd t that f r adults, at about age 11 to 13 While there is no clear dependence of variability of second-formant frequency on particular vowels, the dependence on age wa the same

Summaries of verage ariability typical of each age group f r the first and second f rmant frequencies are shown in Figs. 5 and 6 respectively

Th differences in variability of first formant frequencies am ng the

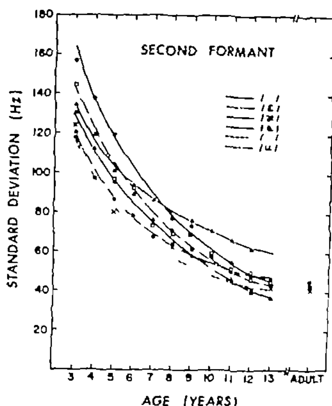


Fig. 6. Intra subject variability in Formant 2 typical of the different age groups as a function of age. In this figure each point represents the square root of the average variance for the children in each age group. The different symbols and the different lines connecting them for each of the six vowels are identified in the key.

vowels are clear here. Variability of [a] is the highest of all vowels while the variabilities of [i] and [u] are the lowest. The variability of first formant frequencies is 140 Hz for [a], 55 Hz for [i] and [u], and 100 Hz for [ɛ], [æ], and [ɔ] at the age of 3. At 13 years, however, it is 35 Hz for [a], 15 Hz for [i] and [u] and 21–29 Hz in [ɛ], [æ] and [ɔ], the same values as those of an adult. The variability of second formant frequencies is approximately the same for all vowels. The variability of second formant frequencies ranged from 120 to 150 Hz at three years and 35 to 57 Hz at thirteen years, reaching adult values.

Ratio of intra subject standard deviation to mean value. It is obvious from *Fig. 5 that the intra subject variability of first formant for [a] is higher* than that for either [i] or [u] but then so is the mean formant frequency. Perhaps variability should be reckoned not as an absolute value but as a fraction of the mean around which the values vary. Accordingly we show *the same data in Fig. but the ordinate describing variability* is the ratio of the standard deviation in Hz to the *child's own mean* first formant frequency. Indeed, the differences among the vowels are less distinct. The decrease with age remains as before.

Fig. 6 showed a fair homogeneity of the absolute variability of the

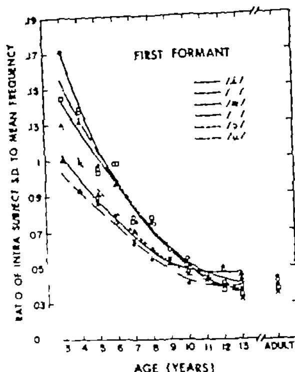


Fig. 7. Re-plotting of first formant data shown in Fig. 5, but with the variability expressed on the ordinate as the ratio of the standard deviation to the mean formant frequency.

second formant for different vowels in absolute terms, but Fig. 8 shows how the relative variabilities separate according to the mean second-formant frequencies.

The relative variabilities for the first formant for the 3-year-olds are still highest for [a] (0.171) and lowest for [i] and [u] (0.098, 0.11). By the age of five or six, however, the ratios are similar for all vowels (0.09 or 0.1) and they remain in the same as they descend to the adult value of 0.03 to 0.05. For the second formant the s.d. mean ratio is lowest for [i] and higher for [a], [ ], and [u], and this finding is independent of age.

Discussion

Acoustical phonetics characterizes phonemes or speech sounds in articulatory terms by places or gestures of the tongue and in acoustic terms by formants and transitions. In the past, studies on vowel formant frequencies have been reported to clarify some acoustical features of speech sounds. It has been recognized that the vowel formants represent the acoustical resonant properties of vocal tract as shaped in articulation by the tongue (Potter, Kopp and Green, 1947; Joos, 1948; Peterson and Barney, 1952;

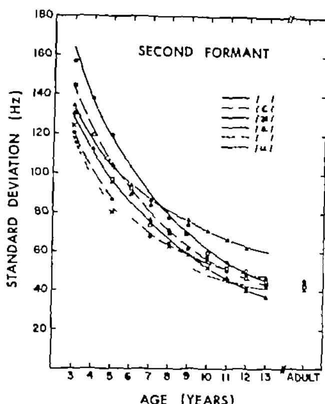


Fig 6 Intra subject variability in Formant 2 typical of the different age group as a function of age In this figure each point represent the square root of the average variance for the children in each age group. The different symbol and the different lines connecting them for each of the six vowel are identified in the key

vowels are clear here. Variability of [a] is the highest of all vowels while the variabilities of [i] and [u] are the lowest The variability of first formant frequencies is 170 Hz for [a], 55 Hz for [i] and [u] and 100 Hz for [ɛ] [ʌ] and [ɔ] at the age of 3 At 13 years, however it is 35 Hz for [a] 15 Hz for [i] and [u] and 21–29 Hz in [ɛ] [ʌ] and [ɔ], the same values as those of an adult The variability of second formant frequencies is approximately the same for all vowels The variability of second formant frequencies ranged from 120 to 150 Hz at three years and 35 to 57 Hz at thirteen years, reaching adult values

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unit length section of the back cavity is larger than the shift caused by a removal of a section of the same length in the middle of the front cavity

F_1 of the vowels [e], [i], and [ɪ] I almost completely determined by the back cavity volume and the narrowest section of the mouth cavity In the vowels [u], [o], and [ ] is somewhat more dependent on the front cavity con triction section. The contribution to F_1 of [u] from the back cavity v lume is somewhat larger than that from the front cavity

The second formant Only in the case of the vowel [i] was the mouth cavity with associated orifices found to be the essential determinant of F_2. F of [i] is clearly a half wavelength resonance of the back cavity There is a similar but not at all so apparent tendency of F of [e] to be influenced *more by the back than by the front cavity* The second formant of the back vowels [u], [o], and [ɑ is somewhat more dependent on the front cavity than on the back cavity Providing the cavity volume changes are introduced on a constant percentage basis, this tendency is apparent, but if the volume changes are performed by means of a constant length reduction there is found an equal dependency of F_2 on the two cavities for [u] and also for [ɑ] In the case of [u], F is dependent much more on the relative dimensions of the tongue pass than on the lip section. These two parts of the compound resonator system have about the same effect on F_2 of both [ɑ] and [o] The lip section is of practically no importance for F of [i] and does not have a very marked influence of [e] either" (Fant, 1960 p 121)

There are only a few studies of vowel formant frequency of children (Pott r and Steinberg, 1950 Peterson and Barney 19 2) especially on the development of form nt frequencies (Potter and Peterson, 1948 Okamura, 1966) What is known is that formant frequencies of eight year old children re about 25% higher than that of adult males and 20% higher than that of adult females.

Okamura (1966) reported, in his study n formant con tructions and differentiation of vowel area in two-formant pace, that Japanese vowel formant frequencies can be differentiated from each other by the age of nine

Needles to say the ocal tract of a child i maller in ize than that of an adult But we cannot ea ily a sume that the formants have higher frequen cies in proportion to th size of the vocal tract with age as a whole because different p rt f the ocal tract presumably change at different rates.

In study on the anat mical development of voice and speech org ns in hildren Negu (1910) pointed ut that the larynx develop most rapidly between th ages of 3 nd 5 years, and then development of the larynx becomes more gradual with ge until puberty is reached.

Our res lt on f rmant frequencies can be summarized as follows

a There i clear decrease of first and second formant frequencies between ages 3 and 5 years.

(b) Generally the decrease f the second-formant frequency is greater than that of the first f rmant frequency

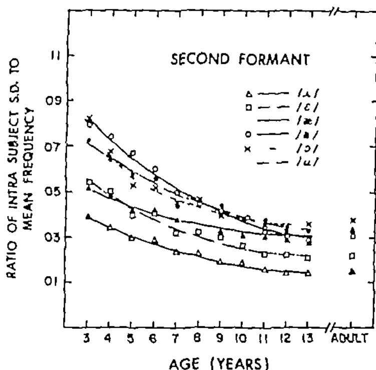


Fig 8 R plotting of second formant d t shown in Fig 6, but with the variability expressed on the rdin te as the rati of the standard deviation to the mean f rmant frequency

Peterson 1951 1959 Potter and Steinberg, 1950 Stevens and House 1961) Identification of the vowel is chiefly dependent on the first and the second formants.

One simple notion from the past was that the first formant corresponds to the back cavity and the second formant corresponds to the front cavity of the mouth (Joos, 1948) However it has also been reported that the formants generated by different talkers speaking the same vowel have different frequencies and that formants generated in producing different vowels may hav the same frequency A theory based on absolute values for vowel formant frequency has great difficulty (Stevens and House 1963) Various investigators have considered as a basis for this confusion size of vocal tract dialect and many other factors

Recent studies of synthesized speech and measurement of the size of vocal tract on X ray pictures reveals that the first and second formants are not simply acoustic features of front cavity and back cavity in the vocal tract (Fant 1960) For example

The first formant The frequency of the first formant F_1 is generally dependent more on the back cavity volume than on the volume of other cavities. An exception is the vowel [a] where F_1 is affected equally on a percentage basis by a change in the front cavity volume and by a change of the back cavity volume Since the back cavity of [a] is much shorter than the front cavity the percentage increase of F_1 due to the removal of a small

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Our result on formant frequ ncies can be summarized as follows

There i a clear decrease of first and second formant frequencies between ges 2 and 3 years.

(b Generally the decrease of the second-formant frequency is greater than that of the first formant frequency

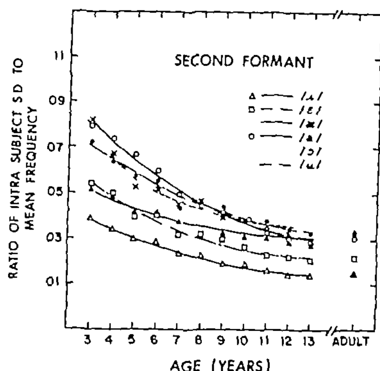


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IV FUNDAMENTAL FREQUENCY

Method

Fundamental frequencies of vowels were estimated from the number of harmonics (up to 4000 Hz) that showed in the narrow band spectrum at the vowel formant sectioning points (Fant, p 241) Earlier attempts were made to use a greatly expanded frequency scale to read the fundamental frequency directly from the spectrogram. That procedure involves an ex panded harmonic line whose thickness offsets any increase in accuracy over the harmonic count

Results

Data for the fundamental frequencies a eraged over all vowels are given in Table 2. The means are based on the 5 repetitions, the 6 vowels, and 5 ubjects in each age group, in short, an averaged fundamental typical of ow l throughout the sentence The between subject S.D. concerns the variation in each age group among the averages of repetitions and vowels. The intra-subject S.D is the variation among the 5 repetitions, averaged (ariance) over all subjects and all vowels. Mean values of fundamental frequencies are shown with between-subject and intra-subject standard deviations in Fig. 9

Mean values Fundamental frequency starting from about 300 Hz at 3 years, decreases slightly with age However the largest decrease of fundamental frequency seems to occur between the ages of 3 and 6 years. Thir teen year-old boys had an average fundamental frequency of 221 1 Hz, still an octav higher than that of adult males (124.2 Hz) Thirteen year-old girls, on the other hand, had an average fundamental frequency of 220 8 Hz, not [illegible] ry different from that of adult females (220 9 Hz)

B tween subject tandard deviation Between-subject standard deviation w s n t dependent n age It ranged from 20 to 45 Hz. Interestingly 13-year ld boy howed a standard deviation of 66.4 Hz, which i a higher [illegible]lue than that found for all other age groups.

Intra-s bject tandard deviation and its relation to mean value Three-yea old children howed about 40 Hz S.D yielding a ratio of standard devi tion t mean of 0 132 There was a gradual decrea ing with age reaching min mum [illegible]lue (12 Hz, 0.04) at age ten or twelve and after that [illegible]e ther wa not further decrease in intra-subject standard deviation of fundam t l frequency (0 04 to 0.05) This decrease in relative variability [illegible] shown in Fig 10

(c) The first formant frequency of [a] is independent of age

(d) Between subject standard deviations of formant frequencies are unrelated to age and sex.

From these results and the work of others (e.g. Negus, and Fant) the following conclusions may be drawn

(e) These acoustical results are in accordance with the rapid anatomical development of the vocal tract between the ages of 3 and 5 years.

(f) The development of the front cavity will have a greater influence on changes in formant frequencies than the development of the back cavity

(g) First formant frequencies of [a] are not so clearly influenced by development of vocal tract but indirectly or mutually influenced by development of front and back cavities, and also other factors (i e fundamental frequency etc)

(h) Variability of formant frequencies for given vowels between subjects is independent of age and sex

Anatomical factors may not be the only source of these variations, since the development of speech sounds in children is influenced also by psycho-physiological development Further the perception of vowels is dependent not only on formant frequency but also on many other information bearing elements of speech (Peterson 1952) We should not expect therefore to understand the development of vowel formant frequency in children on the basis of the anatomical development of vocal tract alone

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Betwe n-subj ct tandard deviation Between-subject tandard deviation wa not dependent on age It ranged from 20 to 45 Hz. Interestingly 13-year-o ld boys howed a standard deviation of 68.4 Hz, which i a higher lue th n that f und for all ther age groups.

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TABLE 2 *Fundamental frequency averaged across all vowels, for the different age groups*

The columns represent the Mean frequency the Between-Subject Standard Deviation, the Intra Subject Standard Deviation and the Ratio of the Intra-S.D to the Mean

Age (yrs.)	Mean	Between-S S.D	Intra-S S.D	Ratio of Intra-S S.D to Mean
3	297 8	30.8	39 2	132
4	285 0	20.0	26.0	091
5	88 7	46.3	22.8	079
6	271 2	27 9	18 4	068
	262.5	33.5	17 7	067
8	261 0	31 1	14 0	054
9	262 5	35.9	13	05?
10	261 0	32.9	1...3	01
11 M	241.2	21 4	10.5	043
11 F	251.5	42.5	12.9	051
1 M	243.2	20.8	10 8	044
12, F	218 0	19.2	10 0	044
13 M	221 1	66 4	9 1	042
13, F	239 8	19 0	9 9	041
Adult M	1 1 2	20.7	5 6	045
Adult F	220 9	10.3	10 1	045

Discussion

It is well known that the fundamental frequencies of children and adult females are higher than those of the adult male The fundamental frequencies of the vowels of an adult female are about one octave higher than that of the adult male Children have a fundamental frequency of about 300 Hz even up to the age of 8 and 10 years. There is no significant difference of fundamental frequency of speech between 7 and 8 years, or between boys and girls of those ages (Fairbanks, Herbert and Hammond 1949 Fairbanks, Wiley and Lassman 1949 Potter and Steinberg 1950 Peterson and Barney 1952)

It is also well known that regulation of fundamental frequency in voice is dependent on many factors, including the length of vocal cord and the regulation of movement of peripheral voice and speech musculature by central nervous system (Pressman, 1942 Kirikae 1943) In his anatomical study \egus (1949) reported that the length of vocal cord is 3 mm at birth 5 5 mm at 1 year 7 5 mm at 5 years, 8 mm at age 8 $^1/_2$ years, 9 5 mm at 15 years, 12.5 to 17 mm in the adult female and 17 to 23 mm in the adult male \ocal cords generally lengthen rapidly up to 6 years and gradually after 6 years.

A study of fundamental frequency and the size of larynx of boys from 12 to 15 years reported that rapid development of larynx, as related to change of voice began at around 13 years and finished at approximately 15 years (Naider 1965)

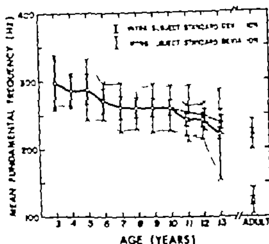
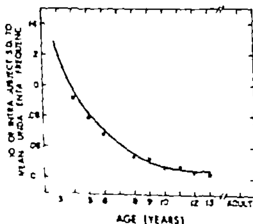


Fig 9 Fund mental frequencies. The open circles re means veraged cross repetitions, ea 1 ad subject 1 each g group The ertical bars enclosed withi horizontal m rkers show the riation (s.d.) acros repetitions, whil those between rrowhead show the riati across subjects. The broken line joins mea for girl onl bo the g of 10 y rs.

The present study shows that fundamental frequency was about 300 Hz at age 3, then there is a remarkable decrease of about 30 Hz between 3 and 6 years, then a gradual decrease after 6 years to 220 Hz in 13-year-old boys. Thirteen year-old girl has an average of 240 Hz, which is not significantly diff rent from that of adult females (220 Hz)

There i a strong correspondence between the fundamental frequency reported here and the changes in the length of vocal cords reported by Negus (1949) Furthermore the fact that between-subject standard deviation



F g 10 V riability i erag f ndamental frequency over repetitions, expressed ratio of 1 me frequency

Table [illegible] *Fundamental frequency* [illegible]

[illegible]

[illegible]	Mean	Between [illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	
[illegible]	[illegible]	[illegible]	[illegible]	
[illegible]	[illegible]	[illegible]	[illegible]	
[illegible]	[illegible]	[illegible]	[illegible]	
[illegible]	[illegible]	[illegible]	[illegible]	
[illegible]	[illegible]	[illegible]	[illegible]	
[illegible]	[illegible]	[illegible]	[illegible]	
[illegible] M	[illegible]	[illegible]	[illegible]	
[illegible] F	[illegible]	[illegible]	[illegible]	
[illegible] M	[illegible]	[illegible]	[illegible]	
[illegible] F	[illegible]	10.2	[illegible]	
[illegible] M	[illegible]	[illegible]	9.4	
[illegible] F	[illegible]	[illegible]	9.9	
Adult M	[illegible]	[illegible]	6	
Adult F	[illegible]	[illegible]	[illegible]	

Discussion

It is well known that the fundamental frequencies of children [illegible] females are higher than those of the adult male. The fundamental [illegible] of the vowels of an adult female are about one octave higher [illegible] of the adult male. Children have a fundamental frequency of [illegible] even up to the age of 8 and 10 years. There is no significant difference [illegible] fundamental frequency of speech between [illegible] and 8 years, or between [illegible] and girls of those ages (Fairbanks, Herbert and Hammond 1949; Fa[illegible] Wiley and Kassman 1940; Potter and Steinberg 1950; Peterson and [illegible] 1952).

It is also well known that regulation of fundamental frequency in [illegible] dependent on many factors, including the length of vocal cord, and the [illegible] ulation of movement of peripheral voice and speech musculature by central nervous system (Grossman 1942; Kirikae 1943). In his anatomical study Negus (1949) reported that the length of vocal cord is 3 mm at birth, 5.5 mm at 1 year, 7.5 mm at 5 years, 8 mm at age 6 ½ years, 9.5 mm [illegible] 15 years, 12.5 to 17 mm in the adult female and 17 to 23 mm in the adult male. Vocal cords generally lengthen rapidly up to 6 years and gradually after 6 years.

A study of fundamental frequency and the size of larynx of boys from 12 to 15 years reported that rapid development of larynx as related to change of voice began at around 13 years and finished at approximately 15 years (Naidor 1965).

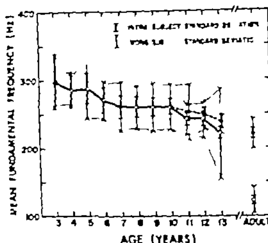


Fig. 9. F adamental frequencies. The open circles re mea eraged across repetitions, words, ad bject l each g group The ertical bars enclosed withi horizont l m kers how the ri tion (s.d.) cross repetitions, while those between rrowhead show the riation across bjects. The broken line joi mea for girl onl boy the ge of 10 years.

The present study shows that fundamental frequency was about 300 Hz at age 3, then there i a remarkable decrease of about 30 Hz between 3 and 6 years, then a gradual decrease after 6 years to 220 Hz in 13-year-old boys. Thirteen-year-old girl have an average of 240 Hz, which is not significantly different from that of adult females (220 Hz)

There is a strong correspondence between the fundamental frequency reported here and the changes in the length of vocal cords reported by N gu (1910 Furthermore the fact that between-subject standard deviation

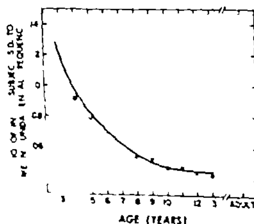


Fig. 10. V i bility i rage f adamental frequency over repetitions, expressed ratio of l me frequency

of thirteen year-old boys was higher than that of other age groups, showed that there are important changes and a rapid decrease of fundamental frequency after about 13 years in boys. This evidence agrees with the results reported by Naider (1965)

In summary fundamental frequency decreases markedly between the ages of 3 and 6 years, after which the decrease is gradual At 13 years, girls have almost the same value of fundamental frequency as adult females, while that of boys still decreases after 13 years rapidly reaching the value of the adult male and corresponding to development of the larynx

V TEMPORAL FEATURES

Method

Wide band spectrograms were used for the measurement of one type of temporal feature in the words. We measured the interval between plosive releases and the subsequent voiced sounds. These time intervals were the gaps between [b] and the release from [l] in the word "blue" between [p] and [ ] in the word "pen" and between [t] and [ɔ] in the word "tall" respectively.

Results

Data for temporal features are summarized in Table 3 and Fig 12.

Mean values The time interval between [p] and [ɛ] in the word "pen" varied from 40 to 68 msec and between [t] and [ɔ] in the word "tall" from 60 to 81 msec N statistically significant difference for the means was found between age groups and therefore we conclude that these time intervals, on the average are independent of age

Between-subject standard deviation Between subject standard deviation of time intervals between [b] and [l] in the word "blue" showed 7.9 to 21.2 msec that of [p] and [ ] in the word pen" 8.5 27 7 msec and that of [t] and [ɔ] in the word "tall 10 4 22.5 msec In this case too the variability among individu ls f r this time interval between phonemes i independent of age

Intra subject variability Three-year-old children showed about 27 msec of intr subject standard deviation and then there was a rapid decrease in ariability as a function f age Variability reached a minimum value (8 10 msec) t age 7 or 8 years, thi alu corresponding to that of adults Here a f r the f rmant frequencies, there is a systematic decrease of indi idual ari bility or n increase in the preci ion of timing, with age Th rial ility reaches it minimum r dult value at a somewhat earlier age than f r the vowel f rmant

Di cussion

There r several studies on ice-onset time and formant-transition time samples of temp oral features of consonant (Lisker and Abramson, 1964 1965 Liberman *et al* 1957 Preston, Yeni Kom hian and Stark, 1967 Ohman 1966) These tudies, which ha e been done on the voice-onset tim f adult peech, rep rted wid variability among subjects. Li ker and Abramson (1965 howed that the mean v ice-onset time of [p] was 8 msec with a range of 20 t 120 msec The mean for [t] wa 70 msec with a range

of thirteen year-old boys was higher than that of other age groups, showed that there are important changes and a rapid decrease of fundamental frequency after about 13 years in boys This evidence agrees with the results reported by Naider (1965)

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Mean data s The time interval between [p] and [ɛ] in the word "pen" varied from 49 to 68 msec and between [t] and [ɔ] in the word "tall" from 60 to 84 msec No statistically significant difference for the means wa found between age groups and therefore we conclude that these time intervals, on the average are independent of age

Between-subject standard deviation Between-subject standard deviation of time intervals between [b] and [l] in the word "blue" showed 7 9 to 21.2 msec that of [p] and [ ] in the word "pen" 8.5–27 7 msec and that of [t] and [ɔ] in the word "tall" 10 4–22.5 msec. In this case too, the variability among individuals for this time interval between phonemes is independent of age

Intra-subject variability Three year-old children showed about 27 msec of intra-subject standard deviation and then there wa a rapid decrease in variability as a function of age Variability reached a minimum value (9–10 msec) at age 7 or 8 years, this value corresponding to that of adults. Here a for the formant frequencies, there is a systematic decrease of individual variability or an increase in the precision of timing, with age Th variability reaches its minimum or adult value at a somewhat earlier age than for the vowel f rmants.

Discussion

There are several studies on voice-onset time and formant-transition time a examples f temporal f atures of consonants (Lisker and Abramson, 1964 1965 Liberman *et al* 1957 Preston, Yeni Komshian and Stark, 1967 Ohman, 1966) These studies, which have been done on the voice-onset t me of adult speech, reported wide variability among subjects. Lisker and Abramson (1965) showed that the mean voice-onset time of [p] was 58 msec with a range of 20 t 120 msec. The mean for [t] was 70 msec, with a range

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In summary fundamental frequency decreases markedly between the ages of 3 and 6 years, after which the decrease is gradual At 13 years, girls have almost the same value of fundamental frequency as adult females, while that of boys still decreases after 13 years rapidly reaching the value of the adult male and corresponding to development of the larynx

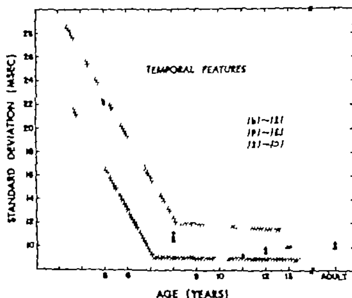


Fig 12 Intra subject s.D. for time interv l specified i the key f nction f ge

same phonetic sequences. These two observations are in accord with those discussed above from other investigators with respect to voice-onset time The new contribution is the systematic decrease in a subject s own variability as age increases. The apparent fact that this temporal feature of speech production reaches an adult-like minimum value at 7 or 8 years while a spectral feature like vowel-formant frequency continues to increase in indi vidual precision to age about 12 years, suggests that the temporal aspect of peech defines phonemic categories earlier and more easily than does a frequency aspect Perhaps this dichotomy strengthen the findings concern ing discrimination at category boundaries, clearer for consonants (Liber man *et al.*, 1957) than for vowels (Stevens *et al* 1964)

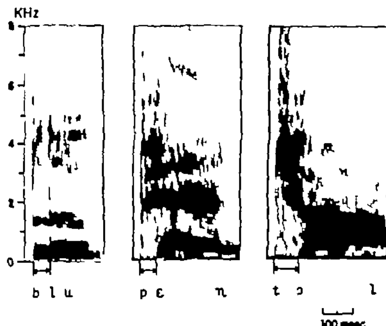


Fig 11 E rtl ns of spectrograms of the words blue "pen and "tall illustrating measurement f time int rval between pl sion and the voiced continuant that foll ws.

of 30 to 105 msec Prestin Yeni Komshian and Stark (1967) reported that the distribution of the values of voice-onset time for children approximated the adult models

The present study shows, with the results summarized above the mean time intervals measured here do not change systematically with age and also that there is wide variation among individuals pronouncing the

TABLE 3 *Time intervals (msec) between plosive sounds and voiced sounds that follow in three different words for all age groups*

Age (yrs.)	b~l Mean	b~l Between S s.D	b~l Intra-S s.D	p~ Mean	p~ Between-S D	p~ Intra S s.D	t~c Mean	t~c Between-S s.D	t~c Intra S s.D
3	3	11 7	27 0	69	12 9	26 1	71	22 5	27 8
4	65	13 9	23 5	60	27 7	19 8	70	18 7	21
5	69	21 2	22.1	68	22 8	17 1	81	21 2	22
6	85	16.5	13 2	65	8 5	17 1	72	10 1	18
7	67	8 5	13 1	40	16.8	11.8	60	11 1	11 1
8	78	11 7	10.8	61	8 8	11 2	0	15.2	10 5
9	67	11 5	10 1	52	10.5	10.8	67	12 1	11 1
10	72	15 6	9 2	61	9 6	10 6	77	15 1	9 9
11	68	17 9	9 3	55	15.1	10.1	65	17 0	9 8
12	68	13 3	9 5	60	12 0	9.9	79	17 2	11 0
13	62	7 9	10.0	56	11 7	10.0	68	14 0	10 0
Adult	70	10 7	9 2	62	16 9	10.3	77	20 1	9 9

TABLE 4 *Display-cards used by listeners with 6 or 12 alternative responses*

1 beet	1	1 beet	1
bet	2	bit	2
æ bat	3	bait	3
bath	4	bet	4
bought	5	æ bat	5
boot	6	bath	6
		bomb	7
		buck	8
		bought	9
		boat	10
		book	11
		boot	12

In order to facilitate the identification of the vowel sample cards on which each vowel was numbered, listed and represented in a key word were distributed to each listener (Table 4) The listener was then to write the number f the identified vowel on an answer sheet 1 retest practice was carried out on 80 items.

Results

A confusion matrix for each age group and listener group was made and the amount of information transmitted by each age group was calculated

Six messages–six responses The results of forced-choice listening with six alternative choices are displayed in the confusion matrix of Table 5 The maximum number in any one cell is th product of 5 children times 5 repetitions times 10 listeners. Inspection of the column totals reveals that while all six stimuli were presented equally often, the six responses were not given equally often Three columns deserve particular notice The choice of [æ] and [ ] a distinct vowel was not a happy one for the dialect of St. Louis. Fig 2 showed that the mean formant frequencies for these two vowel are not ery far part Speakers in this region do not di tinguish clearly the owel in pen and has Furthermore the listeners, including a greater riety of dialects, did not distinguish the two, giving as many as three times the response [ ] a [æ] In addition th low response frequency for [a] probably comes about because in a non Eastern dialect this vowel never exist except as the first part of the diphthong [aɪ] On the response card th [a] was exemplified by the word bath" and the experimenter explained that the word was an example of the sound only in some Eastern dialects wher the wel f "bat, bath and Bob" are all different. Nonetheless, the owel as illustrated on the card does not represent a much used phonemic category in the speech f most of our li teners.

The diagonal cells shows the number of correct identifications out of 250 Expressed as percentages these measures of intelligibility of the six vowels are gi en n Tabl 6 and Fig. 13 for the several ages.

VI IDENTIFICATION OF VOWELS BY ADULT LISTENERS

Method

A long tape containing 1500 randomly distributed vowel samples was used for a listening task These samples were taken from the original recordings and contained vowels produced by the subjects five from age groups 3, 5 7 and 9 years *and ten from age groups 11 13 and adult Half* of each of the three older groups was male and half female

Small segments of tape were cut from the sentence recordings, which segments corresponded to steady unchanging portions of the target vowel according to a listening criterion of the experimenter Not all vowel samples remained steady for the same duration and thus the durations were in fact different ranging from about 100 to 300 msec. According to Joos (1948) criterion for a minimum of 50 msec required for vowel identification all of these samples should have been adequately long A two-way classification analysis of variance of these durations for three widely separated ages showed that the sample durations, averaged over all vowels, were not significantly different for the different ages, but different vowels had different durations, that for [ɔ] being the longest in all cases. There was also a significant interaction between vowel and age

Fortunately for present purposes, the longest durations did not yield the highest intelligibility scores (*vide infra*) For example [ɔ] even though longest in all cases, was not as intelligible as several other vowels. We conclude therefore that in spite of variations in the duration of vowel samples used in the listening tests, such variations did not affect the intelligibility scores The reason probably is that all durations were longer than the minimum necessary

Each sample was followed by a 5 sec segment of blank tape before the next sample was joined Also, during the listening sessions, each block of 80 items was followed by a 2 minute rest period

Twenty normally hearing adults, 12 men and 8 women chosen from *among the training students at Central Institute for the Deaf served as* listeners Ten of twenty listeners had to select an identification response from among six simulus alternatives [i], [ɛ] [æ] [a] [ɔ] and [u] Another ten listeners made identifications among twelve *alternatives [i] [ɪ], [e], [ɛ] [æ],* [a], [ɑ], [ʌ], [ɔ] [o] [ʊ], [u]

Four loudspeakers were hung about 1 5 meters above the heads of listeners seated in two rows. The signal level *at the listener s head* was approximately 70 dB re 0 0002 dyne/cm² at the peak of the speech sound

TABLE 4 *Display-cards used by listeners with 6 or 12 alternative responses*

i	beet	1	i	beet	1
	bet	2		bit	2
æ	bat	3		bait	3
	bath	4		bet	4
ɔ	bought	5	æ	bat	5
u	boot	6		bath	6
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				bought	9
				boat	10
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TABLE 5 *Confusion matrices (6 stimuli and 6 response alternatives) for vowels spoken by subjects at different ages*

Age (yrs.)	Spoken vowel	Identified vowel i	ɛ	æ	ɑ	ɔ	u
3	i	177	32	5		1	33
	ɛ	5	151	22	4	13	3
	æ	7	171	49	8	6	9
	ɑ	1	5	86	85	15	6
	ɔ		1	6	96	139	8
	u	4	14	4	11	13	204
	Total	246	426	172	204	18	263
5	i	183	34	8	1		21
	ɛ	1	191	52			3
	æ	13	185	28	2	1	21
	ɑ	1	26	81	116	8	18
	ɔ	1	2	8	153	70	16
	u	12	20	2	5	4	207
	Total	211	461	1?9	277	63	-89
	i	237	7				6
			180	53	1	2	1
	æ	11	202	29			8
	ɑ		8	61	158	19	1
	ɔ			3	95	150	[illegible]
	u	8			1		-31
	Total	256	414	149	-58	171	[illegible]
9	i	223	18	1	1		
	ɛ	3	212	28	4	2	1
	æ	12	205	9	2	2	20
	ɑ		14	91	132	13	
	ɔ		1	4	92	152	1
	u	2	2			1	215
	Total	240	452	133	231	170	271
11 M	i	168	39				43
	ɛ		191	38	5	6	7
	æ	15	161	10	6	5	41
	ɑ		8	53	148	40	1
	ɔ		2	1	41	201	2
	u	8	1			3	236
	Total	191	408	111	202	258	330
11 F	i	43	4				3
	ɛ	3	217	20	3		
	æ	6	230	8	1	1	4
	ɑ		10	69	144	23	4
	ɔ		2	4	79	161	1
	u	8	1			1	210
	Total	[illegible]	464	101	22	189	250

Age (yrs.)	Spoken vowel	Identified vowel i		æ			
13, M	i	231	12			1	6
			223	20	3	3	1
	æ	8	210	10	3	1	18
			11	75	139	21	1
			18	9	51	172	
		21	5			1	223
	Total	260	479	114	196	202	249
13, F	i	224	17				9
		9	167	57	4	2	11
	æ	16	194	20	3		16
	a		11	78	143	17	1
			1	6	86	187	
		24	7	1		1	217
	Total	273	397	162	236	177	254
Adult, M	i	236	8				6
			183	14	21	9	10
	æ	2	207	18	3	3	17
		2	3	29	173	43	
		1	1	2	17	229	
			1				249
	Total	241	405	63	217	284	278
Adult F	i	233	18				1
		1	201	41	5	1	1
	æ		197	41	7	4	1
			2	36	181	31	
			1	1	82	184	2
		15	2			2	231
	Total	249	419	119	255	222	236

It is clear that intelligibility of all vowels increases with the age of the talker and we assume that this effect is due to the change in variability that characterizes the consistency of repetition of such vowels, as discussed above in the measurement of formant frequencies.

From these values it is also clear that the several vowels are not equally intelligible, [i] and [u] being the highest. On the other hand, these measures of relative intelligibility are contaminated by the response biases discussed above and illustrated by the column totals of Table 5.

Four types of analyses were made on the data of the confusion matrices, shown in Table 5. These were, (*a*) conventional calculation of values of intelligibility indices for each vowel as spoken by each age group (Table 6), (*b*) determination of the amount of information transmitted within each confusion matrix, (*c*) estimation of the pairwise discriminability among

TABLE 6 *Intelligibility of six vowels spoken by subjects of different ages*

Uncorrected scores equal to number of correct responses divided by number of correct responses divided by number of vowels spoken for the six-alternative response The last three rows give averaged results of both sexes in the groups 11 and 13 years, and adult

Age	i	ε	æ	a	o	u	Overall
3	0 8	00 4	19 6	31 0	55 6	81 0	53.6
5	73.2	77 0	11.2	46 1	28.0	82.8	57 2
	91 8	76.0	11 6	63 2	60.0	93 6	66 5
9	89 2	81 8	3 0	52.8	60 8	98 0	61 0
11 M	07 2	77 6	7 0	59 2	81 6	91 1	61 0
11 F	97 2	86.8	3..	57 0	65.6	96.0	6 7
13 M	92.4	89 2	4 0	55.6	68.8	89.2	66 5
13 F	89 6	66.8	8.0	57 2	62.8	86.8	61 9
Adult M	91 4	7 2	7 2	69.2	91 0	90 8	73.2
Adult F	93 2	80 4	16.1	72 1	73 0	92.1	71 1
11 M+F	82.2	82.1	5 1	58 1	73 6	9. 2	60.2
13 M+F	91 0	72 0	0 0	56 1	65.8	88.0	61 2
Adult M+F	93.8	8 8	11 8	70 8	82.6	96 0	72.3

the vowels by use of the Constant Ratio Rule for vowels spoken by all but the two youngest groups, and (*d*) estimation of the probability of a correct identification of each of the vowels as spoken by each age group after applying a correction for response biases

The intelligibility indices for each vowel were calculated by dividing the number of times that vowel was correctly identified by the number of presentations of that vowel These are the measures shown in Table 6 and Fig 13 They demonstrate a general improvement of performance on the identification task as a function of the age of the speakers, for all vowels with the exception of [æ] which apparently was something of a mystery to

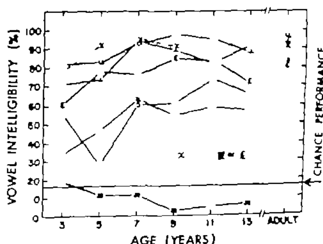


Fig 13 Intelligibility (percentage of items correctly identified) of the different vowels for each of the age groups.

TABLE 7 *Average information transmitted per vowel over all vowels spoken by talkers at different ages.*

Age	IT	Age	IT
3	1.020	11, F	1.609
5	1.109	13, M	1.571
7	1.582	13, F	1.574
9	1.693	Adult, M	1.641
11, M	1.243	Adult, F	1.645

the listeners. (The broken line in this figure i discussed in a later section.)

The amount of information transmitted within each confusion matrix yields a measure of identification performance a eraged across the six owels. This index may thus give a clearer picture of the general improvement in the discriminability of vowels as the speaker s age increases. In formation transmitted (I) was calculated a suggested by Garner and Hake by finding the difference between response information (I) and response equivocation (E) where

$$I = -\sum_{i} p(a) \log_2 p(a)$$

and $$E = -\sum_{i} p(A) \sum_{k}^{m} [p(a_k|A_i) \log_2 p(a|A)]$$

for a matrix of m rows (I) and columns (k). Inf rmation transmitted as a function of age of the speaker (hown in Table 7 Fig 14) reaches close to its maximum value by 7 years.

Consideration of the original confusion matrices demonstrates some problems not treated in the two preceding forms of analysis. As noted earlier the responses were not used equally often, and both information transmitted

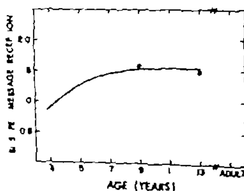


Fig 14. I f rmation transmitted in owel spoken by different ge groups.

TABLE 6 *Intelligibility of six vowels spoken by subjects of different ages*

Uncorrected scores equal to number of correct responses divided by number of correct responses divided by number of vowels spoken for the six alternative response The last three rows give averaged results of both sexes in the groups 11 and 13 years and adult

Age	i	ε	æ	a	ɔ	u	Overall
3	70.8	60 4	19 6	31 0	55 6	81 6	53 6
5	73.2	77 6	11.2	40.4	28.0	82.8	53.
	91 8	76 0	11 6	63.2	60.0	93.6	66 5
9	89 2	84 8	3 6	52.8	60.8	98.0	61 0
11 M	67 2	77 6	7 6	50.2	81 6	91 1	61 6
11 F	97 2	86.8	3 2	57 6	63.6	96 0	67
13, M	92 4	89 2	4 0	55 6	68 8	89 2	66 5
13 F	80 6	66.8	8.0	57 2	62.8	80.8	61 9
Adult, M	94 4	77.2	7 2	69 2	91 6	90 0	3.2
Adult F	97 2	80.1	16.1	72.4	73.0	92.1	1 1
11 M+F	82.2	82 1	5 1	53 4	73 0	93 2	66.2
13 M+F	91 0	72.0	6.0	56 1	65.8	88 0	61 2
Adult M+F	93 8	78.6	11 8	70 8	82 6	90 0	73

the vowels by use of the Constant Ratio Rule for vowels spoken by all but the two youngest groups, and (*d*) estimation of the probability of a correct identification of each of the vowels as spoken by each age group after applying a correction for response biases.

The intelligibility indices for each vowel were calculated by dividing the number of times that vowel was correctly identified by the number of presentations of that vowel These are the measures shown in Table 6 and Fig 13 They demonstrate a general improvement of performance on the identification task as a function of the age of the speakers, for all vowels with the exception of [æ] which apparently was something of a mystery to

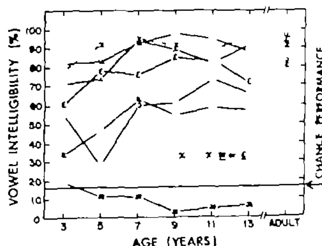


Fig 13 Intelligibilit (p rcent g f t m co rectly id tified) of the d ffere t w l f se en f th g gro ps.

TABLE 7 *Average information transmitted per vowel over all vowels spoken by talkers at different ages*

Age	It	Age	It
3	1.020	11 F	1.699
5	1 169	13, M	1.571
7	1.582	13 F	1.374
9	1.892	Adult, M	1.641
11 M	1.245	Adult, F	1.615

the listeners. (The broken line in this figure is discussed in a later section.)

The amount of information transmitted within each confusion matrix yields a measure of identification performance averaged across the six owels. This index may thus give a clearer picture of the general improvement in the discriminability of vowels as the speaker s age increases In formation transmitted (I) was calculated as suggested by Garner and Hake by finding the difference between response information (I) and response equivocation (E) where

$$I = - \sum p(a) \log_2 p(a)$$

and
$$E_r = - \sum p(A) \sum p(a \mid A) \log_2 p(a \mid A)$$

for a matrix of m rows (i) and columns (k) Information transmitted as a function of age f the speaker (shown in Table 7 Fig 14) reaches close to its maximum value by 7 years.

Consideration of the original confusion matrices demonstrates some problems not treated in the two preceding form of analysis. As noted earlier the responses were not used equally often, and both information transmitted

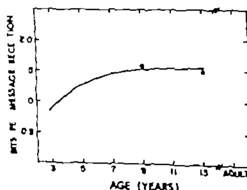


Fig 14 Information tra smitted I ewel spoken by diff rent ge groups.

and intelligibility (simple per cent correct) may be degraded artificially by such response biases That is, even though ability to identify each of the vowels be equal differences in response probability might yield the illusion of real variance in their identifiability That this is not a trivial issue may be seen by examining the relative proportions of the responses [ʌ] and [ɪ] in Table 5 Also it is fairly clear in the original matrices that these same two vowels are never very discriminable one from the other although they do appear to bear information in the sense that either on tends to lead to *one* of the two appropriate responses.

One method for handling these problems is through application of the "Constant Ratio Rule proposed by Clarke (1957) Clarke s rule simply provides that the ratio between any two entries in a row of a submatrix is equal to the ratio between the corresponding two entries in the master matrix In the present case this means that the pairwise discriminability of any two vowels can be estimated from the four entries associated with these vowels in the original six vowel matrix For example the vowels [a] and [ɔ] were correctly identified 1060 and 1262 times, when pronounced by speakers from ages nine through adults (In this analysis we have deleted data for the three younger groups, speakers from which were clearly less precise in their pronunciation than the older speakers) The vowel [a] was identified as [ɔ] 191 times and [ɔ] as [a] 428 times. The constant ratio rule thus predicts that the results of an experiment on the discriminability of these two vowels would yield a matrix of conditional probabilities of the form

		Response /a/	Response /ɔ/
Stimulus	/a/	847	153
	/ɔ/	253	747

It can be seen from this matrix that the response [a] is expected on fifty five per cent of the presentations of a vowel sound while [ɔ] is only ex pected to be used on forty five per cent (more serious imbalances may be found in the original confusion matrices) A now familiar index of discri minability which is relatively independent of such a response bias in the statistic introduced in signal detection theory *d* It is sufficient for this discussion to identify *d* as the separation, in normal deviates, between a pair of overlapping equal variance normal distributions which could give rise to this discrimination matrix (This statistic and its application to confusion matrices has been discussed in detail by Egan (1957)) Another way of ex pressing the discriminability between two such vowels is in terms of the maximum possible per cent of correct identifications (P_{max} (C)) if they were presented equally often This measure is somewhat similar to an intelligibility index *that has been corrected for guessing but it relies* on well-demonstrated relations between response probability and the probability

TABLE 8 *Discriminability (d') within all possible pairs of the 6 vowels spoken (a). Part (b) shows the maximum pairwise discrimination possible in terms of percent correct*

	d'					
	i		æ	a		u
a. *Pairwise discriminability (ages 9–Adult)*						
i	(0)	3.80	2.50	5.00	6.00	3.30
		(0)	−0.28	3.52	4.10	4.20
æ			(0)	1.50	3.28	3.50
				(0)	1 71	5.00
					(0)	4.50
						(0)
b. *Maximum possible pairwise discrimination in terms of % Correct (50 chance performance)*						
i	(50)	97	90	99	99	95
		(50)	41	96	[illegible]	98
æ			(50)	77	93	95
				(50)	80	99
					(50)	99
						(50)

that the responses are correct (as opposed to older techniques which assumed that listeners make pure guesses, i.e. that when wrong they are responding totally independently of the immediate sensory stimulus). The alue of $P_{max}(C)$ is obtained by determining the particular criterion along a decision axis which maximizes the number of correct responses. In the case of equally probably stimuli it is th point where the probability that a given stimulus configuration is a sample from one distribution is the same as the probability that it is from the other. Table 8 a gives the pairwise discriminability between the vowels, as estimated by the constant ratio rule in terms of the tatistic d' for the vowels pronounced by talkers of age nine through adults. Table 8 b presents the same information, but in terms of $P_{max}(C)$. It can be seen from these tables that discriminability among most f the owels was quite good, nearly perfect in many cases. However one of the combinations, [æ] versus [ ], actually produced negative alues of d'. Also the discriminations of [a] from [a] and of [ ] from [æ] are considerably poorer than the othe twelve pairs which yielded positive values of d'.

In a further analysi w used a method similar to that described above to estimat the entries in the discrimination matrices, had they been made with ut response biases. Each of the six-by-six matrices was reduced to six d fferent two-by two matrices by the following technique. For each vowel (x) a matrix was constructed consisting of two rows, the stimulus vowels $\bar{x}$ and "not x" (x) and of two columns, the identifications of x and $\bar{x}$ where x rep esents all vow ls other than x. Values of d' and of $P_{max}(C)$ were

and intelligibility (simple per cent correct) may be degraded artificially by such response biases That is, even though ability to identify each of the vowels be equal, differences in response probability might yield the illusion of real variance in their identifiability That this is not a trivial issue may be seen by examining the relative proportions of the *responses [a] and [ɛ]* in Table 5 Also it is fairly clear in the original matrices that these same two vowels are never very discriminable one from the other although they do appear to bear information in the sense that either on tends to lead to *one* of the two appropriate responses.

One method for handling these problems is through application of the "Constant Ratio Rule proposed by Clarke (1957) Clarke's rule simply provides that the ratio between any two entries in a row of a submatrix is equal to the ratio between the corresponding two entries in the master matrix In the present case this means that the pairwise discriminability of any two vowels can be estimated from the four entries associated with these vowels in the original six vowel matrix For example the vowels [a] and [ɔ] were correctly identified 1060 and 1262 times, when pronounced by speakers from ages nine through adults (In this analysis we have deleted data for the three younger groups, speakers from which were clearly less precise in their pronunciation than the older speakers) The vowel [a] was identified as [ɔ] 191 times and [ɔ] as [a] 428 times. The constant ratio rule *thus predicts that the results of an experiment on the discriminability of* these two vowels would yield a matrix of conditional probabilities of the form

		Response /a/	Response /ɔ/
Stimulu	/a/	817	153
	/ɔ/	.253	747

It can be seen from this matrix that the response [a] is expected on fifty five per cent of the presentations of a vowel sound while [ɔ] is only ex pected to be used on forty five per cent (more serious imbalances may be found in the original confusion matrices) A now familiar index of discri minability which is relatively independent of such a response bias in the statistic introduced in signal detection theory d' It is sufficient for this discussion to identify d' as the separation in normal deviates, between a pair of overlapping equal variance normal distributions which could give rise to this *discrimination matrix (This statistic and its application to confusion* matrices has been discussed in detail by Egan (1957)) Another way of ex pressing the discriminability between two such vowels is in terms of the maximum possible per cent of correct identifications (P_{max} (C)) if they were presented equally ften This measure is somewhat similar to an intelligibility index that has been corrected for "guessing but it relies on well-demonstrated relations between response probability and the probability

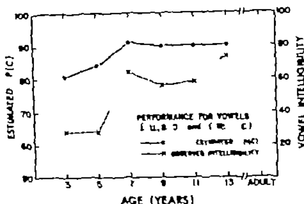


Fig. 16 Estimated percent correct and vowel intelligibility (uncorrected) averaged over f vowel ([æ] and [ ] combined) as f nctio of the ag f the talker

measures for this pair seem to show it to be more accurately identifiable than any single vowel is an example of the misleading effects of response bias.

The values of P_{max} (C) for the combined vowel [æ] or [ɛ], and for the five single vowels were averaged for each age group and are shown in Fig. 16, along with the corresponding averages of the intelligibility scores. These two curves dem n trate fairly clearly that the major improvement of identification performance as a function of the age of the speakers has been com pl ted by age seven and also that the corrected' scores yield a considerably more stable functi n than the raw intelligibility measures. (The P_{max} *(C)* values here are related to the left hand ordinate and the intelligibility scores t the right for reasons indicated earlier.)

Six stimuli, twelve responses

In view of the variability among the speech-sound repetitions, particularly f the younger children, w wished to determine whether certain produced owel sounded to adult like vowels not included in the original set of six. Half f the adult list ners were therefore given 12 alternatives from which t hoose—a set that lmost exhausts the repertory of American English. The results are shown in the confusion matrices of Table 9 The overall intelligibility (ratio f diagonal cells to 250) of the six intended vowels i hown in Table 10 The intelligibility of [I] rises from 42% at age 3 to alues round 0% whil that for [u] starts at 53% The other values are lower except for [ ] whose apparently high intelligibility is confounded by high response frequency for that vowel. The response frequencies for each group can be seen in the column totals in *Table 9* *Note that now many of the* [I] stimuli re alled [ɪ], probably because *of short durations.* Note also that many responses to a and ɔ are distributed under [ɑ] and [ʌ] eh ices not

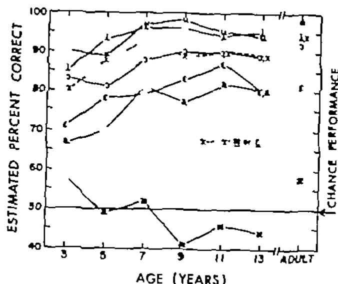


Fig 15 Corrected estimate of intelligibility that takes into account chance performance and the unequal probabilities of response for the different vowels.

determined for each such matrix P_{max} (C) here represents performance estimated under the assumption that x and $\bar{x}$ are presented equally often, rather than with the ratio 1 5 as was actually the case This assumption means only that 50% correct can be regarded as chance performance and it has no effect on the inter relation of the measures for the various vowels.) Fig 15 shows the estimated values of P_{ma} (C) for each vowel as a function of age of the speakers The trend discovered in the original intelligibility measures can be seen slightly more clearly here It is reassuring to see that the major effects are not artifacts associated with response biases

In the analysis using the constant ratio rule to determine the pairwise discriminability of the vowels for the older speakers, it was noted that the vowel [ɛ] was not discriminated from [ɑ] at better than a chance level On further examination it was found that these two were likewise indiscriminable when spoken by the younger groups. Therefore the two vowels were treated as a single one to which either response was considered correct Values of d and P_{ma} (C) were estimated for each age of speaker from the matrices of the form

	or æ	$\overline{\text{or /ɑ/}}$
/ɛ/ or /æ/		
$\overline{\text{/ɛ/ or /ɑ}}$		

and the latter values are shown by the x s which are connected by the dashed line in Fig 15 It can be seen that identification of the pair [ɛ] or [ɑ] is quite accurate at all ages A similar pairing of these two vowels was also made when calculating the initial intelligibility indices, and the results are shown by the dashed line and x s of Fig 13 That the intelligibility

Table 9 (continued)

Age (yrs)	Spoken vowel	Identified vowel											
		i	ɪ			æ			ʌ	ɑ		ʊ	
	a	1	3	4	6	87	21	74	54	23	1	2	2
	ɑ					4	6	64	52	106	17		1
		7	2	1							3	45	192
	Total	206	100	16	309	88	31	142	121	129	23	50	206
13 M	i	171	56	5	2				3		2	2	9
	ɪ		3	3	224	10			8		1	1	
	æ	1	113		97	6			6	1	3	12	10
			8	2	4	69	22	47	59	11			
				3	20	6	6	23	64	113	11	3	
		5	6	1	2						8	49	178
	Total	177	187	14	351	82	28	110	138	123	23	67	197
13 M	i	156	81		3					2		2	6
			71	6	102	49	7	1	3	1	1	4	6
	æ	1	172	4	91	12	5		1			8	3
		1	1	3	15	53	30	90	43	10	1		1
			1		1	2	7	88	12	137	2		
		7	15	3	1	1		1			5	38	179
	Total	165	201	15	218	119	49	178	89	150	10	52	195
Adult, M	i	198	38	1	2								11
			34	4	158	15	9	3	17	4	2	3	1
	æ		34		181	6	1	3	3		8	1	3
				2	1	13	14	129	48	39	2	2	
							1	18	11	174	31		
		1			1						1	16	231
	Total	199	107	14	244	34	25	183	79	217	44	22	248
Adult, F		184	63	9	1	1							2
			18	5	174	38	8		5	1		1	
	æ		7	8	191	17	7	2	6	2	12		1
					1	32	23	152	34	17	1		
					2		8	82	12	139	29		
		1	8						4			35	201
	Total	184	82	19	260	79	44	218	81	159	42	38	207

available to listeners under six alternatives. Finally and again probably reflecting the influence of short durations, many responses to [u] are now [ʊ].

The difficulties in any further analysis of a rectangular instead of a square matrix force us to provide this brief description only. In general the "high" vowels are sometimes identified as their neighboring [i] or [ʊ], and the middle vowels, already less intelligible under six alternatives, show a still more complicated pattern of response.

TABLE 9 *Confusion matrices (6 stimuli and 12 possible responses) for vowels spoken by talkers at different ages*

In this case the talkers had only 6 alternatives to produce while the listeners could choose from among 12 alternatives, the 12 containing the talker's 6 and 6 others.

Age (yrs.)	Spoken vowel	Identified vowel											
		i	ɪ	e	ɛ	æ	a	ɑ	ʌ	ɔ	o	ʊ	u
3	i	106	53	38	15		1		1	1	1	1	22
	ɛ	31	48	20	105	13	4	1	10	4	4	2	
	æ		31	10	133	45	5	3	2	3	9	3	5
	a	2	6	5	31	55	15	69	41	9	1	7	3
	o					1	5	90	31	83	25	4	2
	u	1	5		10	3			1		42	44	133
	Total	140	146	73	297	116	30	163	109	103	81	72	165
5	i	107	85	8	17	8	1		1		2	9	12
	ɛ		21	5	171	37	3		1			3	3
	æ	1	67	6	130	14	7	1	6		2	5	11
	a		5		18	69	20	68	38	5	1	12	14
	o				1	3	6	159	22	38	2	9	10
	u	8	16		3	1			8		9	58	14
	Total	110	191	19	313	132	37	228	70	13	18	96	19
	i	208	30	2	1	5						3	6
	ɛ		14	7	181	35	7		2			1	
	æ	1	85	4	1 1	2_	3		2		3	3	6
	a			1	7	55	11	96	52	22	6		
	o			1	5	3	5	74	51	91	16	1	
	u	7	6	1	1				1		9	1	151
	T tal	216	135	16	319	170	26	170	108	115	31	82	168
0	i	181	52	3	1				1	1		1	1
			23	3	187	23	1	1	6	1	1		1
	æ	1	79	1	130	6	3	1	2		5	11	9
	a					66	31	92	46	17	1		
	o				1		1	86	38	111	5	7	
	u	3	1		1	1					1	65	1 5
	Total	165	155	10	330	08	42	1 0	03	130	16	83	185
11 M	i	121	105	8	4		2	1	1			1	1
	ɛ		10	1	1—	30	6	1	11		[illegible]	1	1
	æ		5	6	96	1	2	1	9	1	15	19	22
	a				10	_5	21	8—	71	30	2	2	
	o				1		4	39	42	110	11	1	1
	u	2	2		1				2	1	13	64	109
	T tal	1_3	203	15	289	61	35	129	135	181	11	8	10
11 F	i	105	46	6	2								1
		1	10	1	103	21	1		6			2	5
	æ	2	89	1	130	6		2			2	1	1

Table 8 (*continued*)

Age (yrs.)	Spoken vowel	Identified vowel											
		i				æ		ɑ	ʌ			ʊ	u
	ɑ	1	3	4	6	87	21	4	58	23	1	2	2
						4	8	61	62	108	17		1
	u	7	2	1							2	45	192
	Total	206	180	18	309	88	31	142	121	129	23	60	208
11, M	i	1 1	58	3	2				3		2	2	9
			5	2	224	10			6		1	1	
	æ	1	115		97	6			5	1	3	12	10
			3	2	6	60	22	87	59	11			
				2	20	6	6	23	65	113	11	3	
	u	5	8	1	2						6	49	178
	Total	177	187	14	331	82	28	110	138	125	23	67	197
13, M	i	158	81		3					2		2	6
			71	5	102	49	7	1	2	1	1	4	8
	æ	1	122	4	84	12	6		1			8	3
		1	1	3	15	53	30	90	42	10	1		1
			1		1	2	7	86	12	137	3		
		7	15	2	1	1		1			5	38	179
	Total	166	291	18	316	119	49	178	59	150	10	53	193
Adult, M	i	198	28	1	2								11
			35	4	158	15	9	3	17	4	2	3	1
	æ		31	7	181	6	1	3	8		8	1	3
				2	1	12	14	129	48	30	2	2	
							1	18	11	174	31		
		1			1						1	16	231
	Total	199	107	14	344	34	25	153	79	217	41	22	248
Adult, F	i	184	63	9	1	1							2
			18	5	174	38	8		5	1		1	
	æ		7	8	191	17	7	2	6	2	12		1
					1	22	23	152	34	17	1		
					2		8	82	12	150	29		
		1	8						4			35	204
	Total	183	82	19	360	79	44	218	61	159	42	36	207

vailable t listeners under six alternatives. Finally and *again probably* reflecting the influence of hort durations, many responses to [u] are now [ʊ]

The difficulties in any further analysis of a rectangular instead of a square matrix force us to *provide this brief* description only In general the "high vowel are som times identified as their neighboring [ɪ] or [ʊ] and the middle vowels, already les intelligible under six alternatives, show a still mo e complicated pattern of response

TABLE 9 *Confusion matrices (6 stimuli and 12 possible responses) for vowels spoken by talkers at different ages*

In this case the talkers had only 6 alternatives to produce while the listeners could choose from among 12 alternatives, the 12 containing the talker's 6 and 6 others.

Age (yrs.)	Spoken vowel	Identified vowel i	ɪ	e	ɛ	æ	ɑ	ɑ	ʌ	ɔ	o	ʊ	u
3	i	106	53	38	15		1		1	1	1	1	22
	ɛ	31	48	20	105	12	4	1	19	4	4	2	
	æ		31	10	133	45	5	3	2	3	4	3	3
	ɑ	2	6	5	31	55	15	69	41	9	4	7	3
	o					1	5	90	31	85	25	4	2
	u	1	5		10	3			12		4	44	133
	Total	140	146	73	297	116	30	163	109	105	81	[illegible]	163
5	i	107	85	8	17	8	1		1		2	9	1
			21	5	174	37	3		4			3	3
	æ	1	67	6	130	14	7	1	6		2	5	11
	ɑ		5		18	69	20	68	38	5	1	12	14
	o				1	3	6	159	22	38		9	10
	u	8	16		3	1			8		9	58	14
	Total	116	191	19	313	132	37	228	79	43	16	96	197
	i	208	30	2	1	5						3	6
	ɛ		14	7	181	35	7		2	–		1	
	æ	1	85	1	121	22	3		2		3	3	6
	ɑ			1		55	11	96	52	27	6		
				1	5	3	5	1	51	91	16	1	
	u	7	6	1	1				1		9	71	151
	Total	218	135	16	319	120	26	170	108	115	31	82	166
9	i	181	32	3	4				1	1		1	1
	ɛ		23	3	187	23	1	1	6	1	1		1
	æ	1	79	4	130	6	3	1			5	11	4
	ɑ				7	66	31	82	40	1	1		
	o				1	2	1	88	38	111	5	7	
	u	3	1		1	1					1	65	1 3
	Total	185	155	10	330	98	1	170	83	130	16	83	158
11 M	i	1 1	103	8	4		2	1	1			1	1
			18	1	177	30	6	1	11		7	1	1
	æ		3	6	96	1	2	1	9	1	15	19	2
	ɑ		2		10	23	21	87	71	30			
	ɔ				1	2	4	30	42	119	11	1	1
										1	17	60	169
	u	2	2		1								
	Total	123	203	15	[illegible]	61	35	170	135	181	11	8	18
													1
11 F	i	193	46	6	2								
		1	40	1	165	21	4	2	6			2	5
	æ	2	89	1	136	6		2			2	1	1

Table 9 (continued)

Age (yrs.)	Spoken vowel	Identified vowel: i				æ	a	ɑ	ʌ	ɔ		c	u
	a	1	3	4	6	57	21	74	88	23	1	2	2
	ɔ					4	6	64	62	106	1		1
		7	2	1							3	45	192
	Total	206	180	14	209	48	31	142	121	129	23	50	205
13, M	i	171	86	5	2				3		2	2	9
			6	3	224	10			6		1	1	
	æ	1	116		97	8			5	1	3	12	10
			3	2	6	60	22	87	59	11			
				3	20	6	6	23	45	113	11	3	
		5	8	1	2						8	49	178
	Total	177	167	14	331	82	28	110	138	125	25	67	197
13, M	i	156	81		3					2		2	6
			71	8	102	49	7	1	3	1	1	4	6
	æ	1	122	4	91	12	8		1			8	3
		1	1	3	15	85	30	90	43	10	1		1
	ɔ		1		1	2	7	88	12	137	3		
		7	15	3	1	1		1			5	28	179
	Total	163	291	15	216	119	49	178	89	140	10	82	193
Adult M	i	198	38	1	2								11
			34	4	158	15	9	3	17	4	2	3	1
	æ		34	7	181	8	1	3	3		8	1	3
				2	1	13	14	129	48	39	2	2	
							1	18	11	174	31		
		1			1						1	16	231
	Total	199	107	14	344	34	23	183	79	217	44	22	248
Adult F	i	184	53	8	1	1							2
			16	5	174	39	8		5	1		1	
	æ		7	4	181	17	7	2	6	2	12		1
					1	22	23	152	34	1	1		
					2		6	62	12	130	29		
		1	6						4			33	204
	Total	183	82	19	309	79	44	218	61	159	42	36	207

available to li t ners under six alternatives. Finally and again probably reflecting the influence of short durations, many responses to [u] are now [ɪ].

The difficulties in any furthe analysis of a rectangular instead of a square matrix force us to provide this brief description only. In general the "high vowels are sometimes identified as their neighboring [ɪ] or [ɛ], and the middle owels, already less intelligible under six alternatives, show a still more complicated pattern of response.

Table 9 *Confusion matrices (6 stimuli and 12 possible responses) for vowels spoken by talkers at different ages*

In this case the talk rs had only 6 alternatives to produce while the listeners could choose from among 12 alternatives, the 12 containing the talker's 6 and 6 others.

Age (yrs)	Spoken vowel	Identified vowel i	ɪ	e		æ	a	ɑ	ʌ	ɔ	o	ʊ	u
3	i	108	53	38	15		1		1	1	1	1	23
	ɛ	31	48	20	105	12	4	1	19	4	4	2	
	æ		34	10	133	45	5	3	2	3	8	3	5
	a	2	0	5	31	53	15	69	41	9	1	7	3
	ɔ					1	5	90	31	85	13	4	2
	u	1	5		10	3			12		12	41	133
	Total	140	146	73	207	116	30	163	109	103	81	72	163
5	i	107	85	8	17	8	1		1		2	9	12
	ɛ		21	5	174	37	3		4			3	3
	æ	1	67	6	130	14	7	1	6		2	5	11
	a		5		18	60	70	68	35	5	1	12	14
	ɔ				1	3	6	150	22	38	2	9	10
	u	8	16		3	1			8		9	58	147
	Total	116	191	19	313	132	37	228	79	13	16	96	197
7	i	208	30		1	5						3	6
	ɛ		14	7	184	35	7		2	2		1	
	æ	1	83	4	121	22	3		2		3	3	6
	a			1	7	55	11	96	52	22	6		
	ɔ			1	5	3	5	71	51	91	16	4	
	u	7	0	1	1				1		9	71	151
	T tal	16	135	16	319	120	26	170	108	115	31	52	166
9	i	181	52	3	4				1	1		1	4
			23	3	187	23	4	1	6	1	1		1
	æ	1	79	1	130	6	3	1	2		5	11	8
	a				7	66	31	82	40	1	1		
	ɔ				1	2	1	86	38	111	5	3	
	u	9	1		1	1					4	65	1 5
	Total	165	155	10	330	98	12	170	93	150	16	83	188
11 M	i	121	105	8	4		2	1	1			1	1
			19	1	177	30	0	1	11		3	1	1
	æ			6	96	1	2	1	8	1	15	10	72
	a				10	25	21	87	71	30	2	2	
					1	2	4	39	12	119	11	1	1
									2	1	13	60	100
	u	2	2		1								
	Total	123	203	15	289	61	35	120	135	181	11	8	197
11 F	i	193	16	6	2								1
	ɛ	1	10	4	163	21	1	2	6			2	5
	æ	3	69	1	136	6		2	7		2	1	1

their further report that if the entries were restricted to those that are identified correctly then the areas of overlap are considerably reduced. Furthermore if now one plots only vowels identified as correct by the talkers themselves, still less overlap is observed (Fairbanks and Grubb, 1961)

With the present results, we assume that a different kind of variability namely variability within subjects that occurs over repetitions, yields less confusion or less overlap as the age of the talker increases. A similar notion is advanced by Okamura (1966) who demonstrated a striking reduction in these areas of overlap as the age of the children increased What is different is that be showed this reduction and consequent improvement in vowel identification in two-dimensional plot of derivations of F_2 and F_3, given by 10 log $F_2/(F_1F_2F_3)^{-3}$ and 10 log $F_3/(F_1F_2F_3)^{-3}$ respectively

TABLE 10 *Intelligibility of 6 vowels spoken by subjects at different ages when the listeners did not know which were 6 alternatives of the talkers, but only that they might have been any of 12*

Age (yrs)	i		æ	a	o	u	Overall
3	42.4	42 0	18 0	6.0	31 0	5 8	32.5
5	42.8	69 6	5 6	8 0	15.2	58.8	33 3
	83.2	73 6	8 8	4 3	36.4	61.5	44 7
9	72.4	74 8	2.4	12 4	44 4	0 0	46 1
11 (♂)	48.3	70 8	1 6	8.4	50.5	[illegible]	4? 7
11 (♀)	78 0	66.0	2.4	8.1	12.1	[illegible]	45 6
13 (♂)	68.4	89.6	2.4	8 7	45 1	1.2	47 6
13 (♀)	62.4	40 8	4 8	12.0	51 8	71 6	48.3
Adult (♂)	79 2	62.1	[illegible]	5 6	69 6	[illegible] 3	51 0
Adult (♀)	73 6	69 6	0.8	9.2	55.6	81 6	49 4

Discussion

The present results on vowel intelligibility agree in several respects with those of previous studies (Peterson and Barney 1952 Miller and Nicely 1955 and Fairbanks and Grubb 1961) Previous intelligibility scores over all vowels are about 75% ranging from 53 to 92% The vowels [i] and [u] appear always to be more intelligible than the middle vowels. The present results for adults show an average intelligibility of 72% with scores of 94 to 96% for [i] and [u] and 70% for [a] The higher scores are associated with only six alternatives while previous studies have mostly used a vocabulary of *from 10 to 12 vowels* The use of 12 alternative responses in the present study does not facilitate the comparison since those responses were to be associated with only six stimulus alternatives

The main effect of course is *that the identification of vowels increases* with the age of the talker no matter whether vowel identification is measured by raw intelligibility scores, by amount of information transmitted or by an estimate of maximum percent correct that is free of listeners response biases. Our interpretation is that particularly in these cases of listening where the listener has no opportunity to tune up to the speech of any talker the intelligibility of vowels depends in part on the consistency with which a given talker utters them This consistency is the inverse of the intra subject variability discussed above The two effects are not completely parallel however since vowel formant variability continues to diminish as age increases to about 12 years, while the listening results reach maximum values for *talker ages of only 7 years*

Variability among vowel formant frequencies is not a new phenomenon Peterson and Barney (1952) displayed graphically the magnitude of variability among talkers by showing areas of overlap on a *Formant 1 Formant 2* plot where exactly the same combination of frequencies represented two different intended vowels Our results on vowel intelligibility agree with

their further report that if the entries were restricted to those that are identified correctly then the areas of overlap are considerably reduced. Furthermore if now one plots only vowels identified as correct by the talkers themselves, still less overlap is observed (Fairbanks and Grubb 1961)

With the present results, we assume that a different kind of variability namely variability within subjects that occurs over repetitions, yields less confusion or less overlap as the age of the talker increases. A similar notion is advanced by Okamura (1966) who demonstrated a striking reduction in these areas of overlap as the age of the children increased. What is different is that he showed this reduction and consequent improvement in vowel identification in two-dimensional plot of derivations of F_2 and F_3, given by $10 \log F\ /(F_1F_2F\ )$ and $10 \log F_3/(F_1F_2F\ )^{-3}$ respectively

VII GENERAL CONCLUSIONS AND DISCUSSION

The results from acoustical measurements of sentences spoken by 84 subjects show that the mean fundamental frequency and the mean first and second formant frequencies change systematically with the age of the talker roughly in accordance with predictions based on anatomical and physiological considerations. Changes in these means are most rapid in those early ages from 3 to 6 years when anatomical change has been noted as most rapid by others

Of greater interest for present purposes was the change in precision or reproducibility of certain aspects of the speech sounds, namely the first and second formants of the vowels and one temporal aspect of the transition from a plosive consonant to the following vowel or semi vowel. Both for mants show a clear decrease in variability on the successive repetitions of sentences for all vowels, though there are differences among the individual vowels in absolute values The implication is clear that 3 year-old children do not move their tongues to exactly the same position for a particular vowel as it occurs in repetitions of the same sentence at least not so exactly the same as older children and adults The varability decreases until about age 11

Similarly the time interval between the explosion of a stop consonant and the following voiced sound is not exactly repeated time after time but rather shows a certain variability This variability decreases from a maxi mum value at 3 years (the youngest age tested) to a minimum value at about age 8 somewhat earlier than was the case for minimum variability in the vowel formants

The impetus for the present study came from observations of both authors on the intelligibility of speech of children in the countries where the authors second languages were spoken observations quite closely related to the concept of "phonemic category as required in a motor theory of speech perception Foreigners appear to have more difficulty understanding the speech of native children than do native speakers. If this difficulty is related to inaccuracy or sloppiness in the reproduction of the sounds of language, then it would appear that at least children s speech cannot be well described by relatively fixed sound categories The present results on the decrease of this variability with age imply that a motor theory of speech perception must somehow be restricted to adults and older children where speech sounds can be regarded as relatively distinct habits

Concepts of motor behavior controlled in part by sensory feedback are as old as the distinction between sensory and motor systems made around

1811 by Bell and Magendie Early theories concerned voluntary movement and the idea was extended to nonvoluntary systems especially under the name of homeostasis.

Control of a motor system from sensory information arising in the motor system itself has been likened to the servo-system developed in several aspects of engineering theory (MacColl, 1945 Wiener 1948 Shannon and Weaver 1949 Davis, 1951 Peterson, 1953 Fairbanks, 1954 Brown and Campbell, 1948 Mysak, 1959 1966)

The sensory information that is utilized for control of speech production arises in several sensory modalities. While there is much current interest in the forms of feedback from the musculature and articulating surfaces of the speech mechanism, we assume that the principal modality is auditory We believe that our results illustrate the rather large error signals that arise in the early years of speech production, but also that the subsequent formation of rather fixed articulatory habits of position and of gesture involves smaller error signals and perhaps even less dependence on sensory feedback. That the feedback never goes to zero in normal talkers is shown by the deterioration of speech that follows the onset of moderate to severe losses of hearing

In order for the auditory system to provide information about error to the speech-production system, the deviations in the speech output must, of course be discriminated in hearing With respect to the adult values for variability of formant frequencies, shown in Figs. 3-8, one might ask why does there remain an average global standard deviation of about 25 Hz for the first formant, and about 40 Hz for the second formant Surely listeners can detect changes in the frequency of a pure tone that are smaller On the other hand, changes in the peak region or formant of a complex tone are somewhat more difficult to discriminate as was shown by Flanagan (1955) Using the MIT POVO speech synthesizer he created artificial vowels in which one formant at a time could be varied in frequency By presenting pairs of vowels in which either F_1 or F_2 was different, he obtained difference limens or just-noticeable differences of the order of 25 Hz for the first formant and about 40–80 Hz for the second formant, the latter depending more on the value of the comparison F_2. In short the present variability measures in speech production are about as low as they could be if discriminable differences to the ear were the controlling or limiting factor

It is not at all clear how perceptual discrimination develops. In the child's younger years, when his formant frequencies are so much more variable than those of the adult would his formant discrimination be similarly poor Though formant discrimination has not been tested in young children, some recent observation on temporal features may provide a clue

Variability in the time interval between the explosion in a plosive consonant and the voicing that follows, as illustrated in Fig 12, reaches a minimum value (standard deviation) for the adult of approximately 10 msec This rather precise performance in a language that contains only two

VII GENERAL CONCLUSIONS AND DISCUSSION

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Concepts of motor behavior controlled in part by sensory feedback are as old as the distinction between sensory and motor systems made around

SUMMARY

Sound spectrograms were made of recordings of standard sentences spoken by each of 84 subjects—children ranging in age from 3 to 13 years, and adults. Sentences were repeated by each subject five times. Acoustical measures and statistical calculations concerned fundamental frequency and the first and second formant of vowels, and interphonemic temporal features of words. Adult listeners identified vowel segments taken from the recordings of several age groups.

Intra-subject variability, that is, the acoustical repeatability of certain sounds in the sentences, for the vowel formant frequencies decreases as the age of the talker increases to 11 or 13 years. At least one interphonemic temporal feature also shows a decrease in variability with age, but it reaches its minimum at an earlier age, 7 or 8 years. Intelligibility of the vowels for adult listeners also increases with the age of the talker, reaching maximum values for talkers of ages 8 or 9 years. Other results show changes in the mean fundamental frequency and the mean formant frequencies with age.

Relations between these results and anatomical-physiological development are discussed, as are also relations to language learning and phonemic categories.

SOMMAIRE

On a enregistré (magnetophone) des phrases parlées par chacun des 84 sujets, de l'âge 3 ans jusqu'à l'âge de 13 ans, et adultes. Chaque *sujet* a répété les phrases 5 fois. Les mesures acoustiques tirées des spectrogrammes, et les calculs statistiques ont concerné la fréquence fondamentale, les *formants* des voyelles, et certaines intervalles interphonémiques. De plus, des auditeurs adultes ont identifié les voyelles.

La variabilité intra-sujet pour les formants — c'est-à-dire l'inverse de la précision de la répétition des sons dans les phrases — décroit avec l'augmentation de l'âge du locuteur jusqu'à l'âge de 11 ou 13 ans, dès que la valeur est égale à la valeur adulte. La variabilité des intervales temporales entre les consonnes plosives et les voyelles suivantes décroit aussi avec l'âge, mais le minimum apparait à l'âge de 7 ou 8 ans.

L'intelligibilité des voyelles pour les auditeurs adultes s'augmente avec l'âge des locuteurs, mais celle-la achève le maximum dès l'âge de 8 ou 9 ans. Des autres resultats concernent la changement avec l'âge des moyens des fréquences fondamentales et des fréquences formantes.

classes of plosive consonants, is necessary for some of the sharp distinctions involved in separating voiced from voiceless consonants. Such discrimination, however, appears already in the listening behavior of 3-year-old children according to Winterkorn *et al.* (1967) who showed that such children accepted as "da" only those synthetic syllables with voice-onset time of 20 msec or less, and as "ta" those stimuli with 45 msec or more. But this is at an age when the present results show very great variability (Fig. 12) with standard deviations as large as 20–28 msec.

While this line of evidence is neither abundant nor simple, it appears that the variability under investigation in the present work is descriptive more of the motor control process than of perceptual capability at different ages.

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Des rapports entre ces resultats et le développement anatomique et physiologique ainsi que le développement du language et les catégories phonémiques, compriment la base de la discussion

ZUSAMMENFASSUNG

Sprachspektrogramme von Sätzenaufnahmen gesprochen von 84 Versuchspersonen im Alter von 3 bis 13 Jahren waren gemacht Jede Versuchsperson wiederholte die Sätze fünfmal Akustische Messungen und statistische Berechnungen der Grundfrequenz der Stimme der ersten und zweiten Formantfrequenzen der Vokale und der interphonemischer Zeitcharakteristiken waren durchgeführt Vokalsegmente, die aus den originalen Aufnahmen von verschiedenen Altersgruppen genommen waren, waren mit erwachsenen Zuhorern identifiziert

Die Intraversuchspersonvariabilitat das heisst der Mangel der akustischen Wiederholungsfähigkeit einiger Laute in Sätzen, für die Formantfrequenzen der Vokale vermindert sich als das Alter zu 11 oder 13 Jahre steigt Es vermindert sich mit dem Alter die Variabilität auch wenigstens einer interphonemischen Zeitcharakteristike diese reicht aber Minimum im Alter von 7 bis 8 Jahren Auch die Verständlichkeit der Vokale die mit erwachsenen Zuhörern geprüft war steigt mit dem Alter des Sprechers, und reicht maximale Werte bei 8 bis 9-jährigen Sprechern Es waren dargestellt andere Ergebnisse die die Veränderung der mittleren Grundfrequenz der Stimme und der mittleren Formantfrequenzen zeigen

Die Verhältnisse zwischen diesen Ergebnissen und der anatomisch physiologischen Entwicklung so wie auch das Verhaltnis zum Lernen der Sprache und zu phonemischen Kategorien sind gezeigt

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SUPPLEMENTUM 2[illegible]

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INTRODUCTION

There are still pending a number of problems concerning functional disorders of the pharynx and esophagus noted on radiological examination. The etiology and pathogenesis of the majority of these phenomena are not clear and it cannot be determined whether some of them should be considered normal phenomena or pathological phenomena.

The purpose of this paper is to appraise clinical significance of these functional disorders by examining the relationships between them and organic lesions of the pharyngo esophageal region including the connected nervous system, and by investigating the incidence of these phenomena in normal persons of different age categories.

Under the term functional disorders of the pharynx and esophagus is included disorders of deglutition at the level of the pharynx, and dyskinesias and dystonias of the esophagus found radiologically. In the present study following eleven phenomena are discussed i. e. hesitant deglutition, pharyngeal stasis, piecemeal deglutition, pharyngeal laxity asymmetrical deglutition, regurgitation into the epipharynx, aspiration into the trachea, pharyngo esophageal spasm, regurgitation into the pharynx, tertiary contractions and functional diverticula.

RESULTS AND COMMENT

Hesitant Deglutition

Hesitant deglutition consists of difficulty in moving the barium bolus from the oral cavity to the pharynx. The barium bolus is stagnant on the back of the tongue, and many swallowing movements must be repeated before the bolus is projected into the pharynx. Sutherland (1962) described that this particular form of dysphagia takes two or more swallows to force the food out of the mouth or in severer cases no matter how much the food is chewed it goes "round and round" but won t go down.

In the present study hesitant deglutition was observed in only three cases aged more than 60 years in the normal group as shown in Table I. Its degree in these normal cases was slight, and no dysphagia for ordinary foods was complained of Considering the fact that the phenomenon is observed in the normal group in only aged persons, it is presumed that the phenomenon may be ascribed to a tendency to xerosis in the oral cavity resulting from senile atrophy of the mucous membrane and to latent hypokinesia in swallowing

In the clinical group as shown in Table 2, this sign was observed in 23 cases. It occured most frequently in cases with pharyngeal paralysis, suggesting that it is one of the most important radiological signs of paralytic disease of the pharynx. This sign was observed in six cases with malignant tumors, and is considered to be due to the decreased swallowing function accompanied by general debility (Fig. 1 2). Furthermore, hesitant deglutition was found in one case of ulcerous

TABLE 1 *Incidence of the functional disorders of the pharynx and esophagus in normal subjects*

Age	Number	Hesitant deglutition	Pharyngeal stasis	Asymmetrical deglutition	Tertiary contractions
21 30	20	0	2	2	2
31 40	20	0	3	1	4
41 50	20	0		3	8
51 60	20	0	7	2	10
Over 61	20	3	16	2	11
Total	100	3	30	10	35

METHOD

Subjects are divided into a normal group and a clinical group The normal group compromises 100 healthy persons who have no subjective symptoms and show no pathological findings on otolaryngologic examination There are five subgroups of 20 persons each aged 21 to 30 years, 31 to 40 years 41 to 50 years, 51 to 60 years and more than 60 years The clinical group consists of 258 patients who have any subjective symptoms in the pharynx or esophagus and who have been proven to have any organic disease which causes their subjective symptoms.

Fluoroscopic examination was carried out in all cases and fluoro scopic views considered to be useful were supplemented by fixed X ray films. When required cine fluorography was accomplished and the findings were examined subsequently All of the subjects were examined in standing position and supine position each by anterior lateral right anterior oblique and left anterior oblique projections. The radioopaque medium used in this study was Bargin S_1● which contains 78 1 g of barium sulfate per 100 ml The dose for a single swallow was kept almost constant.

RESULTS AND COMMENT

Hesitant Deglutition

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41 50	20	0	2	3	8
51 60	20	0	7	2	10
Over 61	20	3	16	2	14
Total	100	3	30	10	38

METHOD

Subjects are divided into a normal group and a clinical group. The normal group compromises 100 healthy persons who have no subjective symptoms and show no pathological findings on otolaryngologic examination. There are five subgroups of 20 persons each aged 21 to 30 years, 31 to 40 years, 41 to 50 years, 51 to 60 years and more than 60 years. The clinical group consists of 258 patients who have any subjective symptoms in the pharynx or esophagus, and who have been proven to have any organic disease which causes their subjective symptoms.

Fluoroscopic examination was carried out in all cases, and fluoroscopic views considered to be useful were supplemented by fixed X ray films. When required cine fluorography was accomplished and the findings were examined subsequently. All of the subjects were examined in standing position and supine position each by anterior, lateral, right anterior oblique and left anterior oblique projections. The radioopaque medium used in this study was Bargin S_1* which contains 78.1 g of barium sulfate per 100 ml. The dose for a single swallow was kept almost constant.

disorders of the pharynx and esophagus

Asymmetrical deglutition	Regurgitation into the epipharynx	Aspiration into the trachea	Pharyngeal spasm	Regurgitation into the epipharynx	Tertiary contractions	Functional diverticula
1		1			1	
	1					
5	1	2			1	
1						
1		3			2	
		2				
2		1				
2		3			1	1
3		5			2	
		1		2	6	
					3	
2		1			1	1
1		1				
1					3	1
1		1			12	1
					2	
1						
4					2	1
					1	
2			3		2	1
1					3	
					2	
		1			1	
					1	
3						
					15	

gators as one of the important radiological findings in malignant tumors of the upper digestive canal as well as one of the most common symptoms in pharyngeal neuromuscular disorders.

In the present study pharyngeal stasis was found in 30 of 100 normal subjects (Table 1). It occured more frequently in the two advanced age groups than other groups. Especially in the group aged more than 60 years, 16 subjects out of 20, or 80 per cent, showed the stagnation. Table 3 indicates the localization of stagnation in the normal subjects. The barium residues tended to stagnate more frequently in the vallecula than the piriform sinuses. Simultaneous stagnation at both areas was found in 9 subjects, most of them being more than 60

TABLE 2. *Incidene of the functiona*

Clinical diagnosis	Number	Hesitant deglutition	Pharyngeal stasis	Piecemeal deglutition	Pharyngea laxity
Progressive bulbar paralysis	1	1	1		
Pseudobulbar paralysis	3	2	3	1	
Parkinson's disease	2		2	1	1
Pharyngeal paralysis	14	10	13	5	5
Amyotrophic lateral sclerosis	1	1	1	1	1
Recurrent paralysis	5		2	1	
Posticus paralysis	3		2		
Cancer of the hypopharynx	3	1	2		
Cancer of the larynx	5		o		
Cancer of the cervical esophagus	18	–	14	4	
Cancer of the thoracic esophagus	28	1	4	1	
Cardiac cancer	9		3	1	
Thyroid cancer	3	1	3	1	
Mediastinal tumor	–	1	2	1	
Hypopharyngeal diverticulum	6		5		
Esophagitis of the cervical portion	19		6		
Esophagitis of the thoracic portion	10		1		
Peptic esophagitis	2	1	1		
Esophageal varix	9				
Periesophageal abscess	2				
Esophageal diverticulum	27		3		
Esophageal stricture	2				
Achalasia	19		1		
So-called cardiospasm	7		2		
Plummer Vinson syndrome	9	1	1	1	
Aortitis with or without aneurysmal dilatation	9				
Aberrant right subclavian artery	5		1		
Dermatomyositis	1	1	1	1	
Duodenal ulcer	1			1	
Cervical spondylosis	30		5		

esophagitis in one case of dermatomyositis and in one case of Plummer Vinson syndrome. Of these the case of Plummer Vinson syndrome was accompanied by pharyngeal spasm and severe xerostomia with smooth tongue.

Pharyngeal Stasis

Pharyngeal stasis is characterized by stagnation of the barium residues in the vallecula and the piriform fossae or either of them in spite of several complementary swallowing movements following the first This sign was first reported as "dysphagia atonica" by Holzknecht and Olbert (1910), and subsequently has been noted by many investi

disorders of the pharynx and esophagus

Asymmetrical deglutition	Regurgitation into the epipharynx	Aspiration into the trachea	Pharyngeal spasm	Regurgitation into the epipharyn	Tertiary contractions	Functional diverticula
1		1			1	
	1					
5	1	2			1	
1						
1		3			2	
		2				
2		1				
2		3			1	1
3		5			2	
		1		2	6	
					3	
2		1			1	1
1		1				
1					3	1
1		1			12	1
					2	
1						
2						
4					2	1
					1	
2			3		2	1
1					3	
					2	
		1			1	
					1	
3					15	

gators as one of the important radiological findings in malignant tumors of the upper digestive canal as well as one of the most common symptoms in pharyngeal neuromuscular disorders.

In the present study pharyngeal stasis was found in 30 of 100 normal subjects (Table 1). It occured more frequently in the two advanced age groups than other groups. Especially in the group aged more than 60 years, 16 subjects out of 20, or 80 per cent, showed the stagnation. Table 3 indicates the localization of stagnation in the normal subjects. The barium residues tended to stagnate more frequently in the vallecula than the piriform sinuses. Simultaneous stagnation at both areas was found in 9 subjects, most of them being more than 60



Fig. 1. Anteroposterior view Barium stasis in the oral cavity and valleculae, in a man aged 67 years, suffering from cancer of the thoracic esophagus.

TABLE 3 *Incidence of vallecular stasis and piriformis stasis in normal subjects*

Age	Number	Vallecular stasis	Piriformis stasis
21-30	2	1	1
31-40	3	3	0
41-50	2	2	0
51-60	7	6	2
Over 61	16	15	9
Total	30	27	12

years of age As was mentioned by Lindsay (1955), in advanced senility there may be atrophy and hypokinesia of the pharyngeal muscles and less smooth co ordination of the swallowing movements which causes stagnation of food or barium in the vallecula and piriform sinuses.

In the clinical group pharyngeal stasis was observed in 83 cases out of 258 or 32 per cent indicating that this phenomenon is the



Fig. 2. Anteroposterior iew. Barium stasis in the oral cavity and aspiration into the trachea, in woman aged 62 years, suffering from postcricoid cancer.

most common sign of the kinetic disorders of the pharynx (Table 2). Almost all cases of neurological disease with pharyngo-esophageal symptoms, such as progressive bulbar paralysis, pseudobulbar paralysis, Parkinson's disease, pharyngeal paralysis and amyotrophic lateral sclerosis showed this sign (Fig. 4, 5). It was noted that in these neurological diseases the stasis was accompanied frequently by other dyskinetic phenomena such as hesitant deglutition, piecemeal deglutition, pharyngeal laxity etc. It is also interesting to note that stasis was observed in 4 cases of 8 suffering from recurrent laryngeal nerve paralysis.

Furthermore this phenomenon was observed in various organic lesions of the hypopharynx and upper esophagus such as malignant tumors, hypopharyngeal diverticula, cervical esophagitis, periesophageal abscess, cervical spondylosis etc. (Fig. 1, 6, 7, 8, 9, 10). It is presumed that these organic lesions, except for diverticula, increase the resistance at the affected areas against the passage of barium bolus, which induces its stagnation. The fact that this condition occurs almost exclusively



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Age	Number	Vallecular stasis	Piriformis stasis
21-30	2	1	1
31-40	3	3	0
41-50	2	[illegible]	0
51-60	7	6	[illegible]
Over 61	16	15	0
Total	30	27	1

years of age. As was mentioned by Lindsay (1955), in advanced senility there may be atrophy and hypokinesia of the pharyngeal muscles and less smooth co-ordination of the swallowing movements which causes stagnation of food or barium in the vallecula and piriform sinuses.

In the clinical group pharyngeal stasis was observed in 83 cases out of 258 or 32 per cent indicating that this phenomenon is the



Fig. 4. Anteroposterior view during Valsalva manoeuver. Barium stasis in the valleculae and piriform sinuses, in a man aged 65 years, suffering from paralysis of the pharynx. The hypopharynx is markedly distended with air; the barium enters the larynx.

also observed in several cases of malignant tumors of the cervical esophagus and other regions.

Pharyngeal Laxity

Pharyngeal laxity is represented by dilatation of the pharynx on radiographic studies. The pharyngeal cavity dilates laterally and forward remarkably and gives a patulous, atonic, sac like appearance in the anteroposterior view. When the Valsalva manoeuver is carried out, this phenomenon is much more apparent than in the resting phase. Thus, the examination for this phenomenon ought to be carried out in the resting phase and at the time of the Valsalva manoeuver.

In our study the condition was observed in 5 cases of pharyngeal paralysis, in one case of Parkinson's disease and in one case of amyotrophic lateral sclerosis, all of them being associated with pharyngeal stasis (Table 2 and Fig. 4).

Pharyngeal laxity is due to a decrease in pharyngeal tonus and its existence can be reliable evidence of neurogenic disorders of the swallowing mechanism.



Fig. 3. Anteroposterior view Barium stasis in the valleculae and right piriformis sinus, in a woman aged 45 years. Note the phenomenon of asymmetrical deglutition, which in this case appears to have no pathological significance.

in lesions of the pharynx and upper esophagus and seldom in those of the middle and lower esophagus may support this assumption For the cases with hypopharyngeal diverticula the stasis is considered to result from decreased intrapharyngeal pressure during swallowing

Piecemeal Deglutition

Piecemeal deglutition represents the phenomenon in which barium bolus is not pushed into the esophagus as a whole by a single swallowing but is moved in separate small quantities by several successive swallowing movements.

This phenomenon was not observed in the normal group In the clinical group it was observed in patients with pharyngeal paralysis, pseudobulbar paralysis, Parkinson s disease amyotrophic lateral sclerosis and recurrent laryngeal nerve paralysis mostly accompaning hesitant deglutition pharyngeal stasis or pharyngeal laxity (Table 2). It was



Fig. 6. Asymmetrical degl tition, in man ged 68 years, suffering from cancer of the cervical esophagus. Left Anteropost rior view during the active phase Right Right lateral iew during the resting phase Barium stagnates markedly in the valleculae and piriform sinuses

it is essential to ensure that the patient is placed in the true antero posterior position in order to derive from this sign its true diagnostic value.

In the clinical group as presented in Table 2, this sign was ob served in 8 cases of neurogenic lesions, 10 cases of malignant tumors localized to the pharyngo esophageal region, 4 cases of esophageal diverticula 3 cases of cervical spondylosis, 2 cases of Plummer Vinson syndrome and in some other cases (Fig 5 6 9 11 12). Since this condition is observed not rarely in normal subjects, it is difficult to confirm that the condition is a pathognomic sign of any disease. However when this sign is found along with other functional disorders such as hesitant deglutition piecemeal deglutition tracheal aspiration and if neurogenic disorders can be excluded, development of a malig nant tumor involving the pharynx larynx and cervical esophagus is strongly suspected.

Regu gitation into the Epipharynx

Regurgitation of barium into the epipharynx is one of the most



Fig 5. Anteroposterior view Barium stasis in the piriform sinuses and asymmetrical deglutition in a man aged 58 years, suffering from pseudobulbar paralysis.

Asymmetrical Deglutition

In normal persons a barium bolus is ordinarily observed to pass symmetrically from the piriform sinus on both sides to the esophagus in the anteroposterior projection of the fluoroscopic examination Asymmetrical deglutition is characterized by an asymmetrical or one sided passage of the bolus through the piriform sinuses.

In the present study this sign was found about 10 per cent of the time in every age category of the normal group (*Table 1*). *No age* predominance was noted in the incidence of this phenomenon In these normal subjects the asymmetrical sign disappeared when they extended the neck of the obstructed side On the contrary when a normal person without asymmetrical deglutition turn his head to one side at the time of swallowing the passage of the barium bolus through the piriform sinus of that side is hindered Those facts show that the occurrence of the phenomenon is closely related with asymmetry of the tonus of the neck muscles Therefore as was noted by Brombart



Fig. 6. Asymmetrical deglutition, in man aged 66 years suffering from cancer of the cervical esophagus. Left: Anteroposterior view during the active phase. Right: Right lateral view during the resting phase. Barium stagnates markedly in the valleculae and piriform sinuses.

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Regurgitation into the Epipharynx

Regurgitation of barium into the epipharynx is one of the most



Fig. 7 Anteroposterior view Barium stasis in the valleculae and piriform sinuses, in a man aged 49 years suffering from postericoid cancer

common signs in patients with velar insufficiency and is observed readily on lateral projection In the present study however this sign was observed in only 2 cases, one case of Parkinson's disease and one case of pharyngeal paralysis (Fig 14).

Aspiration into the Trachea

Aspiration of barium into the trachea was first observed fluoroscopically by Landau (1923). This phenomenon is induced by insufficient closure of the laryngeal aperture resulting from neurogenic obstacles or organic diseases. Bachman (1959) classified the causes of this phenomenon as follows

A. Abnormalities of neurogenic origin
  1 Faulty timing of the stages with respect to passage of the bolus.
  2. Inability of the various furrows to close completely and form an effective seal against the leakage of fluid past them
  3 Inability of the various furrows to remain closed for the entire period during which the swallowed fluid is passing by

B Organic diseases in the laryngopharynx



Fig. 8. Ant roposterior view during Valsalva manoeuver. Barium stasis in the valleculae and lateral hypopharyngeal diverticulum, in man aged 51 years, complaining of slight dysphagia.

1. Mechanical obstruction of a mass.
2. Limited mobility of arytenoids or epiglottic folds due to neoplastic or inflammatory infiltration.
3. Surgical procedures on the laryngopharynx.

In our series this phenomenon was not observed in the normal group. It was observed in 8 cases of neurogenic lesions and 12 cases of neoplastic tumors (Fig. – 11). In addition one case of cervical esophagitis and one case of dermatomyositis showed this sign. It should be noted that this sign was always accompanied by pharyngeal stasis.

Pharyngo Esophageal Spasm

Spasm of the pharyngo esophageal sphincter is observed fluoroscopically as a depression or indentation of the posterior wall of the hypopharynx at the level of the body of the sixth or seventh cervical vertebra. This finding is observed not rarely during radioscopic examination in patients without any pharyngeal complaint, and it is difficult



Fig. 9. Anteroposterior view Asymmetrical deglutition, in a man aged 50 years suffering from cervical spondylosis.

to attribute to it any pathological significance. Brunner (1952) postulated that a transitory hypopharyngeal bar is due to spastic contraction of the cricopharyngous muscle while the spontaneous, or permanent hypopharyngeal bar is caused by permanent contracture of the crico pharyngeal muscle

In our experience this condition was recognized in 3 cases of Plummer Vinson syndrome one of them being accompanied by meso pharyngeal spasm (Fig 13).

Considerable difference of opinion is expressed in regard to the main pathologic findings accepted as the cause of dysphagia in the Plummer Vinson syndrome Müller and Csipö (1962) claimed that dys phagia in the Plummer Vinson syndrome is due to dryness of the pharyngo esophgeal mucous membrane and spasm of the cricopharyngeal muscle On the contrary Brombart stressed diffuse esophagitis with chronic inflammatory infiltration and the formation of semilunar membranes or webs inserted on the anterior wall of the hypopharynx immediately below the cricoid cartilage McNab Johnes (1961) described



Fig. 10. Anteroposterior view. Barium stasis i the valleculae in man aged 75 years, suffering from cervical spondylosis.

that there were 19 cases with an abnormal barium swallow out of 39 cases radiologically examined. It was possible to get a satisfactory follow up in 17 of these 19 cases. He observed typical web formation in the hypopharynx in 12 of 17 cases. In the remaining 5 cases there was well marked persistent spasm and narrowing of the hypopharynx, but no web formation.

Regurgitation into the Pharynx

The barium bolus, after moving into the esophagus once, flows back into the pharynx again. This sign was observed in our series only in 2 cases of cancer of the thoracic esophagus. The appearance of this sign in these cases is attributed to the stenosis of the esophagus at the level of the lesions and the decrease in tonus of the pharyngo esophageal sphincter

Tertiary Contractions

In early papers (Cannon 190" Carlson and Luckhardt 1914



Fig 9 Anteroposterior view Asymmetrical deglutition in a man aged 50 years suffering from cervical spondylosis.

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Fig. 12. Anteroposterior view in cinefluorography. Asymmetrical deglutition in a man aged 61 years, suffering from cancer of the cervical esophagus. Left and center: Asymmetrical deglutition during the active phase of deglutition. Right: Barium stasis in the valleculae after cessation of deglutition.

Curling is usually asymptomatic but may produce esophageal pain. Templeton (1948) did not consider this type of contraction to be entirely normal, as they are not seen often in younger age groups, but are encountered frequently in older individuals.

In accordance with Templeton's observation, the results obtained from our series of normal subjects shows that the sign was rare in the age groups younger than 40 years, but was more and more frequently encountered among older individuals (Table 1).

In the clinical group this sign was observed in various lesions. Table 2 shows that cervical esophagitis and cervical spondylosis are the lesions which cause this condition most frequently (Fig. 15, 16, 17).

Tertiary contractions are observed almost exclusively at the level below the aortic arch of the esophagus and quite exceptionally at any higher level. Cinefluoroscopic examination revealed that the duration of the contractions ranged from 1.1 seconds to 11.9 seconds, most of



Fig. 11 Anteroposterior view Asymmetrical deglutition and aspiration into the trachea, in a man aged 61 years suffering from hypopharyngeal cancer

Jurica 1926) this phenomenon was reported as tertiay peristalsis or localized contractions. Thereafter various names such as curling rippl ing Kräuselung intermittent spasms transitory autonomic contractions *and tertiary contractions have been given to this phenomenon Its* fluoroscopic appearance is characterized by simultaneous irregular con tractions of the distended esophagus in the portion below the level of the aortic arch. *At the height of the contraction* the lumen *assumes a* peculiar irregular serrated appearance The contractions may be only fleeting or may last for several seconds. They are usually accompanied *by a tonic phase which diffusely* narrows the lumen (Templeton 1948). Brombart described that there is a surge of irregular very close con tractions generally invading the lower two thirds or three quarters of *the esophagus, following* each other with such rapidity that they appear to occur simultaneously

Sheinmel et al. (1949) described this sign as follows (1) Curling is uncommon but not rare (2) Curling is believed to be produced by incoordinated unrelated segmental spasms of the smooth muscle. (3)

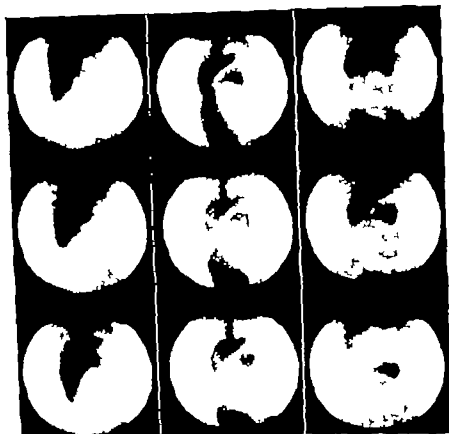


Fig. 12. Anteroposterior view in cinefluorography. Asymmetrical deglutition in man aged 61 years, suffering from cancer of the cervical esophagus. Left and center: Asymmetrical deglutition during the active phase of deglutition. Right: Barium stands in the valleculae after cessation of deglutition.

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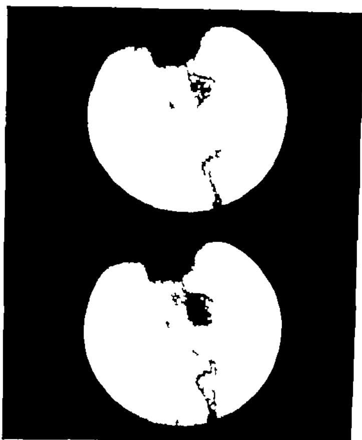


Fig. 13. Anteroposterior view in cinefluorography during the active phase of deglutition. Spasms are observed simultaneously at the level of the mesopharynx and pharyngo-esophageal junction in a woman aged 4_ years suffering from Plummer Vinson syndrome

them being between 2 and 5 seconds (Fig 18).

As to the time relationship between the occurrence of this phenomenon and primary peristalsis of the esophagus the following three types were observed (1) occurrence at the semi evacuation stage of the esophagus after the passage of primary peristalsis, (2) occurrence just after the passage of primary peristalsis, (3) occurrence simultaneously with primary peristalsis. Of these the first type was most frequently encountered

The mechanism of this type of contractions has not been made clear Since the phenomenon is peculiar to the smooth muscle portion of the esophagus and is observed more frequently in older individuals, it is presumed that the phenomenon is a sign of a neuromuscular incoordination of the esophagus.

Functional Diverticula (Tired Spasms)

The present phenomenon was first reported by Bársony in 1926 as functional diverticula and thereafter various terms such as false diverticula tired spasms pearl necklace esophagus and corkscrew esophagus



Fig. 14. Right lateral view in cinefluorography. Regurgitation into the epipharynx, in a man aged 81 years, suffering from paralysis of the pharynx.



Fig. 15. Right anterior oblique view. Tertiary contractions in the lower two-thirds of the thoracic esophagus in the same case as in Fig. 10.

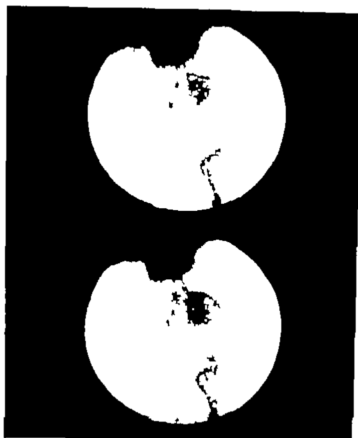


Fig. 13. Anteroposterior view in cinefluorography during the active phase of deglutition. Spasms are observed simultaneously at the level of the mesopharynx and pharyngo-esophageal junction in a woman aged 42 years, suffering from Plummer Vinson syndrome.

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Fig 17 Tertiary contractions in woman ged 4. years suff ring from esophagitis of the cervical portion. Left In the right anterior oblique iew the ppearances of the lower two-third of the esophagus, t the instant when tertiary contractions make their ppearance. Right The same iew; smooth outline fter tertiary contractions ha ceased.



Fig. 16. Right anterior oblique view. Tertiary contractions in the lower two-thirds of the thoracic esophagus, in a man aged 70 years, suffering from esophagitis of the cervical portion.

were also used for this phenomenon.

Several symmetrical and circular contractions occur simultaneously in a part of the esophagus accompanied by round diverticulum like swellings between the strictures, taking on the appearance of a neck lace of large beads. It appears suddenly, lasts several seconds and disappears suddenly again. After its disappearance the esophagus resumes a smooth and straight outline. Similarly to tertiary contractions, this condition occurs almost exclusively in the subaortic part of the esophagus. It is noted that when the phenomenon occurs repeatedly in a patient, each diverticulum like swelling is apt to appear almost at the same place in the esophagus.

In the present study, functional diverticula were not found in any normal subjects. They were observed in 6 patients, representing



Fig. 17. Tertiary contractions in woman aged 43 years, suffering from esophagitis of the cervical portion. Left: In the right anterior oblique view: the appearances of the lower two-thirds of the esophagus, at the instant when tertiary contractions make their appearance. *Right*: The same view; *smooth outline* after tertiary contractions have ceased.

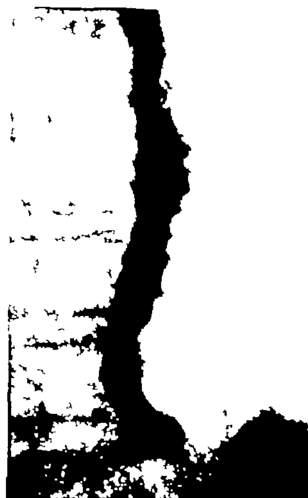


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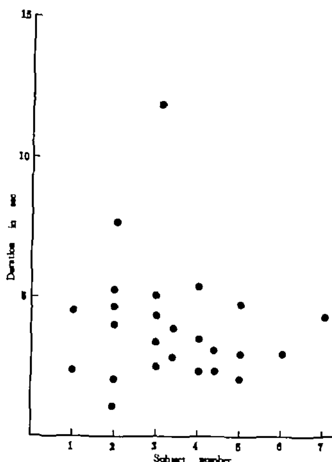


Fig 18. Duration of tertiary contractions measured by means of cinefluorography in 7 patients.

one case each with laryngeal cancer thyroid cancer hypopharyngeal diverticula cervical esophagitis, esophageal diverticula and Plummer Vinson syndrome respectively The patients ranged in age from 43 to 67 years, and complained of dysphagia in 3 cases, discomfort in the sternal region in one case feeling of esophageal stenosis in one case and pharyngeal pain in one case partly being due to the accompanying pharyngo esophageal lesions (*Fig 19 20 21 22*). *Brombart reported* that this phenomenon is nearly always accompanied by dysphagia and as soon as the spasms occur the patient is painfully aware of them

The genesis of functional diverticula still remains obscure, as is the case with tertiary contractions. Bárony and Polgár (1927) noted that this phenomenon can occur reflexly from affections of the stomach and duodenum Brombart confirmed the fact and stated that the very frequent association of esophageal dyskinesias with ulcers of the duodenum forms a very valuable argument in favour of the hypothesis



Fig. 10. Right anterior oblique view. Functional diverticula in the lower third of the esophagus, in man aged 61 years, complaining of substernal distress.

that tertiary contractions and functional diverticula are due to a nervous condition or to a neuromuscular incoordination dependent on some reflex. Ungerecht (1963) also indicated frequent occurrence of this phenomenon in patients with true esophgeal diverticulum, hiatus hernia, esophagitis, gastric ulcer duodenal ulcer cholecystitis, and diseases of the heart and the vessels.

Tertiary contractions and functional diverticula bear similarities in their preferred age and site of occurrence. However a definite difference between them exists with regard to incidence. Functional diverticula are not found in normal persons, whereas tertiary contractions are rather common phenomena, at least in old individuals.



Fig. 20. Functional diverticula and permanent diverticulum in a woman aged 43 years complaining of slight dysphagia. Left: Right anterior oblique view of functional diverticula during the extreme stage of contraction. Right: Anteroposterior view during resting phase; the bulge persists after cessation of functional diverticula as permanent diverticulum.

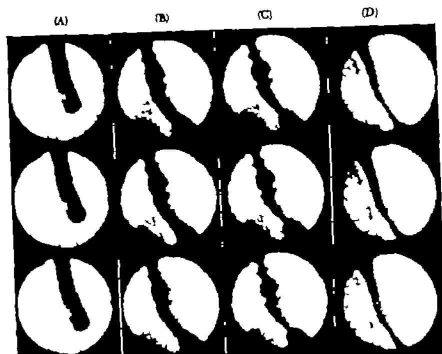


Fig. 21. Right anterior oblique view in cinefluorography in woman aged 64 years, suffering from diverticulum of the cervical esophagus. (A) Advance of the primary peristaltic wave in the lower third of the esophagus. (B) and (C): Immediately after the passage of the wave functional diverticula are beginning to appear and become very markedly (D): Smooth outlines after their disappearance.

Classification of the Functional Disorders of the Pharynx and the Esophagus

On the basis of results obtained from our study the above mentioned eleven functional disorders are classified into the following four categories from the standpoint of their incidences.

1. Those observed in normal adults, especially in older age groups: pharyngeal stasis, tertiary contractions.
2. Those observed in normal adults uniformly at all ages: asymmetrical deglutition.
3. Those observed rarely in normal persons hesitant deglutition.
4. Those never observed in normal persons: piecemeal deglutition pharyngeal laxity regurgitation into the epipharynx, aspiration into the trachea, pharyngo-esophageal spasm, regurgitation into the pharynx, functional diverticula.



Fig. 20. Functional diverticula and permanent diverticulum in a woman aged 43 years, complaining of slight dysphagia. Left Right anterior oblique view functional diverticula during the extreme stage of contraction. Right Anteroposterior view during resting phase the bulge persists after cessation of functional diverticula as permanent diverticulum.

SUMMARY

For the purpose of evaluating clinical significance of functional orders of the pharynx and esophagus, the authors investigated oroscopic findings of 100 normal healthy persons, and 258 patients h pharyngo-esophageal lesions.

The results obtained lead to the following conclusions:

1 Hesitant deglutition, pharyngeal stasis, piecemeal deglutition, aryngeal laxity and aspiration into the trachea are important findings central or peripheral paralysis of deglutitory function In the jority of cases, two or more phenomena are observed simultaneously a same patient.

2. Pharyngeal stasis is observed in normal subjects, especially in ler age groups. In these normal cases, the phenomenon is considered sign of subclinical hypokinesia of swallowing.

3. Pharyngeal stasis and asymmetrical deglutition are often im rtant indirect radiologic findings in malignant tumors of the hypo arynx or cervical esophagus.

4. When asymmetrical deglutition is observed, an imbalance of e tonus of the left and right neck muscles should be kept in mind.

5. Tertiary contractions are observed frequently in normal indivi uals of higher ages.

6. Functional diverticula are rather rare phenomena, observed clusively in patients with organic lesions of the pharynx, esophagus other parts of the digestive tract.



Fig. 22. Right anterior oblique view. Functional diverticula of the esophagus in a woman aged 67 years, complaining of slight dysphagia after laryngectomy.

SUMMARY

For the purpose of evaluating clinical significance of functional disorders of the pharynx and esophagus, the authors investigated fluoroscopic findings of 100 normal, healthy persons, and 258 patients with pharyngo-esophageal lesions.

The results obtained lead to the following conclusions:

1 Hesitant deglutition, pharyngeal stasis, piecemeal deglutition, pharyngeal laxity and aspiration into the trachea are important findings in central or peripheral paralysis of deglutitory function. In the majority of cases, two or more phenomena are observed simultaneously in a same patient.

2. Pharyngeal stasis is observed in normal subjects especially in older age groups. In these normal cases, the phenomenon is considered a sign of subclinical hypokinesia of swallowing.

3. Pharyngeal stasis and asymmetrical deglutition are often important indirect radiologic findings in malignant tumors of the hypopharynx or cervical esophagus.

4. When asymmetrical deglutition is observed an imbalance of the tonus of the left and right neck muscles should be kept in mind.

5 Tertiary contractions are observed frequently in normal individuals of higher ages.

6. Functional diverticula are rather rare phenomena, observed exclusively in patients with organic lesions of the pharynx, esophagus or other parts of the digestive tract.

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The authors would like to express their appreciation to Dr Roger C. Breslau United States Air Force Hospital Tachikawa for his careful review of the manuscript.

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The Otological Research Laboratories, Department of Otolaryngology The Ohio State University College of Medicine, Columbus, Ohio, U.S.A

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Director of Otological Research Laboratories,
Assistant Professor of Otolaryngology
Ohio State University Columbus

With the technical help of Wyman C. Lane, B.Met.E.,
The Battelle Memorial Institute,
Columbus Laboratories, Columbus

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E N D BY

Almqvist & Wiksells

BOKTRYCKERI AKTIEBOLAG

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CONTENTS

INTRODUCTION

Since 1951 when the electron microscope was first employed for otologic investigation a wealth of information concerning the fine structure of the inner ear has become available. Outstanding contributions have been made by Carlström and Engström (1955), Engström (1951), Engström and Wersäll (1953a, 1953b, 1958a and 1958b), Engström and Sjöstrand (1954), Friedmann (1959 and 1962), Iurato (1961 and 1967), Iurato and de Petris (1967), Smith (1956, 1957 and 1961), Smith and Sjöstrand (1961), Hilding (1965), Kimura (1966), Kimura, Schuknecht and Sando (1964), Duvall, Flock and Wersäll (1968), and Spoendlin (1964 and 1966) as well as others.

A surface preparation technique using osmium fixed temporal bones, recently employed in the light microscopic investigation of the inner ear (Engström, Ades and Andersson, 1966; Johnsson and Hawkins, 1967a and 1967b) has added a new dimension to otological research. These studies, however, have been limited by the resolving power of the light microscope. An improved instrument with higher resolving power than that of the conventional microscope was desirable for investigation of surface preparations.

A new type of microscope—a scanning electron microscope (SEM)—which has been widely used in metallurgical investigations is now available for biomedical research. Unlike the conventional electron microscope which transmits an electron beam through the specimen, the image in the scanning microscope is created by secondary electrons emitted from the excited surface of the specimen. The result is a picture similar to the image produced on a television screen, a cathode ray tube. The depth of field obtained with the scanning microscope is about 500 times that of a light microscope. The magnification ranges between ×20 and ×20 000 with a resolving power of 100 Å.

During the last several years, biological specimens studied with this new microscope have included such diverse material as cultured cells, human chromosomes, cell organelles, skeletal material, blood cells, and cancer cells, (Hayes, 1968). This paper reports on the efforts of the authors to study the general surface architecture of the cochlea and vestibular sensory organs of guinea pigs using the scanning electron microscope.

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MATERIAL AND METHODS

Ten young guinea pigs weighing between 300 and 400 grams were used in this study Their temporal bones were removed immediately after sacrifice and fixed for one hour in phosphate-buffered osmic acid The bones were rinsed thoroughly with Ringer s solution and then a graded alcoholic dehydration was carried out The bony shell of the cochlea was removed with the aid of a surgical microscope at the stage of 70 alcohol Each of the separated portions of the membranous cochlea and the vestibular organs were mounted on the aluminum microscope stage with Aquadag (carbon suspension in alcohol) and coated with gold The gold coating provided a conductive surface on the otherwise non-conductive specimen All of the important areas were photographed and examined stereoscopically thereby providing a three dimensional appreciation of the structural morphology A limited number of osmium fixed specimens of the vestibular sensory organs were treated with 10% hydrochloric acid for one to five minutes and then thoroughly washed with distilled water This treatment dissolves the gelatinous otolithic membrane covering the sensory epithelium and uncovers the hairs of the sensory cells

FINDINGS

A Cochlea (Figs 1 and 2)

Stria vascularis and its adjacent structures

A complex vascular network can be clearly appreciated in the stria vascularis The vessels continue freely from the scala vestibuli area into the stria vascularis (Fig 3) Epithelial cells covering the stria vascularis were equiaxed and hexagonal Small depressions and numerous microvilli were noted on the epithelial surface of the stria vascularis (Fig. 4) These microdepressions were interpreted as microvesicles of the epithelial cells. Occasionally nuclei and intracellular inclusions were shown as well rounded protrusions The size and shape of the epithelial cells of the stria vascularis was interrupted suddenly at the attachment of Reissner s membrane This regular cellular arrangement observed in the stria vascularis was less pronounced in the epithelial cells lining the scala vestibuli

The cellular arrangements of the spiral prominence were of great interest Cells covering the upper margins of the spiral prominence were elongated hexagons with their long axis parallel to the plane of the basilar membrane (Fig. 5) The cells covering the central portion of the prominence were smaller equiaxed hexagons than those observed in the stria

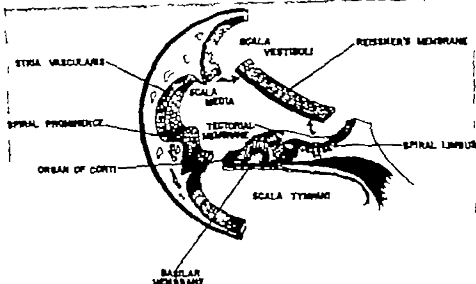


Fig. 1 A schematic diagram illustrating how the cochlea was prepared. Reissner membrane w removed to expose the underlying structures. The stri scalaris nd its adjacent struct re were separated from the temporal bone The tectorial membrane was partiall or totally removed. (Drawing by B. Etter)

Fig. 2. A photomicrograph of the cochlea indicating rea studied. *1* Stria vasculari and it adjacent structure; *2*, spiral limbus *3* tectorial membrane *4* organ of Corti *5* myelinated nerv fibers t the osseo spiral lamina.

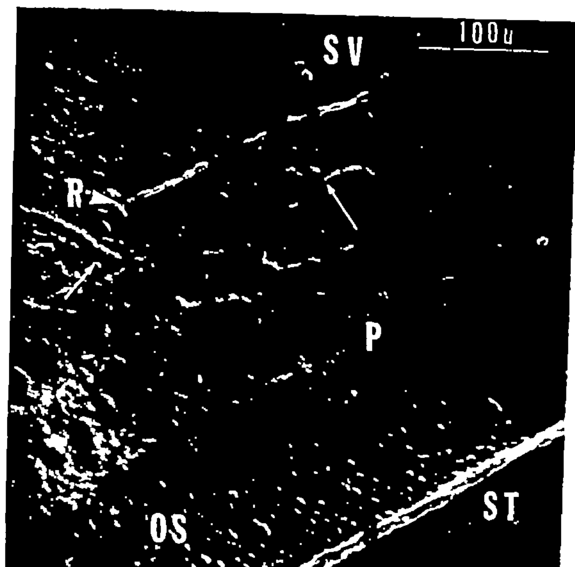


Fig 3 A scanning photomicrograph showing the entire stria vascularis and its adjacent structures. Arrows indicate the tortuous course of vessel in the stria vascularis. *R* Reissner's membrane insertion *P* spiral prominence *OS* outer sulcus cell *B* basilar membrane; SV scala vestibuli *ST* scala tympani

vascularis The size of the epithelial cells covering the lower margin of the prominence became larger and at the margin of the outer sulcus cells the hexagonal cell surface could no longer be distinguished (Fig. 6) This cell arrangement was noticed in all of the four turns except at the blind ends of the cochlear duct where the spiral prominence faded away

Cells covering the *scala vestibuli* and *scala tympani* were also examined The surfaces of these cells were hexagons but their margins were much less distinct than that found in the stria vascularis Some areas revealed a mesh like fibrous arrangement immediately under a thin layer of epithelial cells (Fig 7 A and B) The mesh like structure was interpreted as the spiral ligament

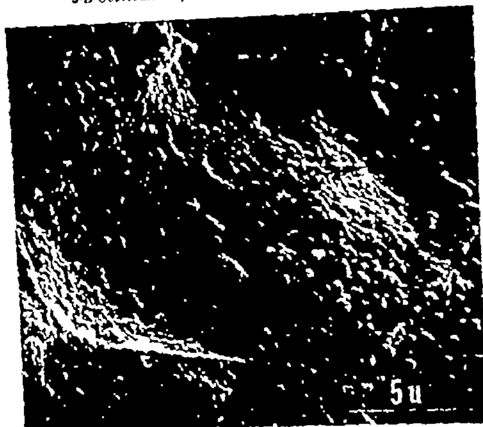


Fig. 4. \ highe mag ification f epithelial cell of the stria vascularis. Observ the microdepression on the cell surface (arrow) which are interpreted the vesicles f the electron microscopic findi g. The m lti-ped ocolated small structures re microvilli.

Limbus spiralis

The limbu spiralis wa studied in order to discover how the tectorial membrane was attached. The cell arrangement in this region was not clear except in a few instances where the tectorial membrane attachment was extremely thin. In a few instances, depression similar to volcanic craters were observed. Sometimes, these structures were oriented parallel to the line of the estibular lip where the tectorial membrane contacts the limbus and they seemed t be more pronounced in the apical turn than in the basal turn (Fig. 8 A and B). These craters varied considerably from one anim l to nother. When plastic embedded sections were examined by phase contrast and electron microscopes, it was clearly demonstrated that thi crater f rmation showed different stages of development and was outlined by interdental cell membranes. The interdental cell membrane forming the craters revealed well developed microvilli. The opening of the crater to the endolymphatic space sometimes contained a residue of tec t rial-membrane substance (Fig. 9).

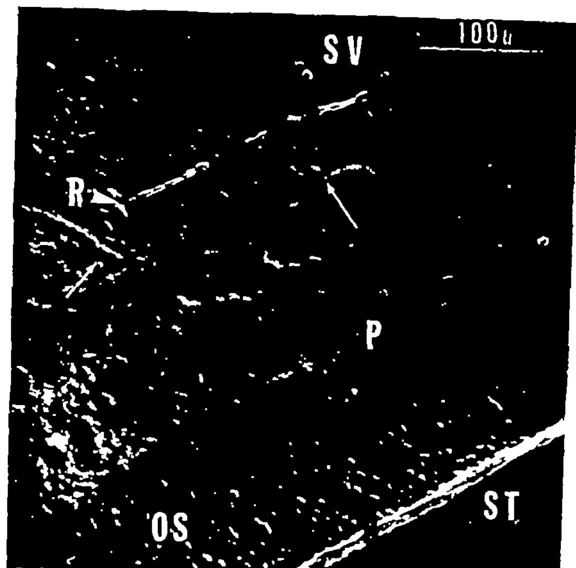


Fig 3 A scanning photomicrograph showing the entire stria vascularis and its adjacent structures. Arrow indicates the tortuous course of vessels in the stria vascularis. *R* Reissner membrane in section *P* spiral prominence *OS* outer sulcus cell *B* basilar membrane *SV* scala vestibuli *ST* scala tympani

vascularis The size of the epithelial cells covering the lower margin of the prominence became larger and at the margin of the outer sulcus cells the hexagonal cell surface could no longer be distinguished (Fig 6) This cell arrangement was noticed in all of the four turns except at the blind ends of the cochlear duct where the spiral prominence faded away

Cells covering the scala vestibuli and scala tympani were also examined The surfaces of these cells were hexagons but their margins were much less distinct than that found in the stria vascularis Some areas revealed a mesh like fibrous arrangement immediately under a thin layer of epithelial cells (Fig A and B) *The mesh like structure was interpreted as the* spiral ligament

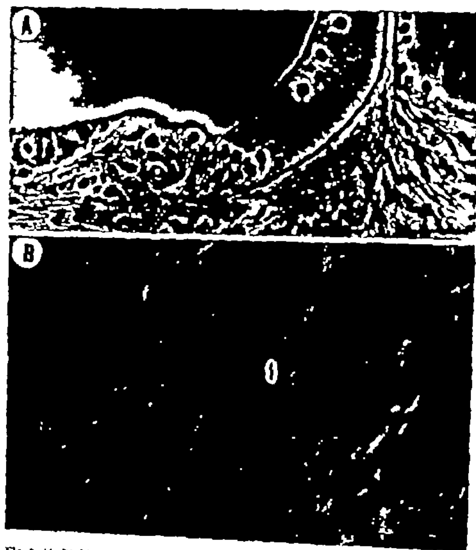


Fig. 8. (A, B) *Phase contrast* and scanning photomicrographs illustrate the junction between the spiral prominence and outer sulcus cell (O). Observe the irregular cell surface of the outer sulcus cells. Their cell boundaries are not distinct. The border between root cell and outer sulcus cell is indicated with arrow.

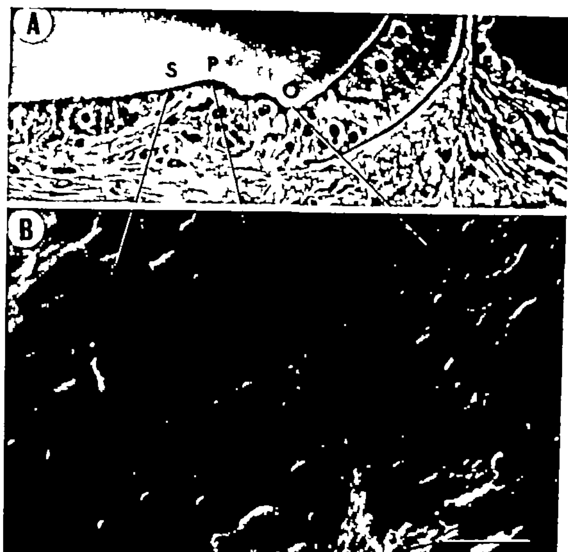


Fig 5 (A) A phase contra t micrograph of the spiral prominence area Arrows indicate similar areas in th scanni g micrograph B. S Margin f tri vascul ri O m rgin of outer ulcu cells P piral prominence (B) A survey micrograph f th rea h w in the abo e ph se co trast micrograph. Observe lifferences of cell pattern in I m g th se rea indicated with rrows.

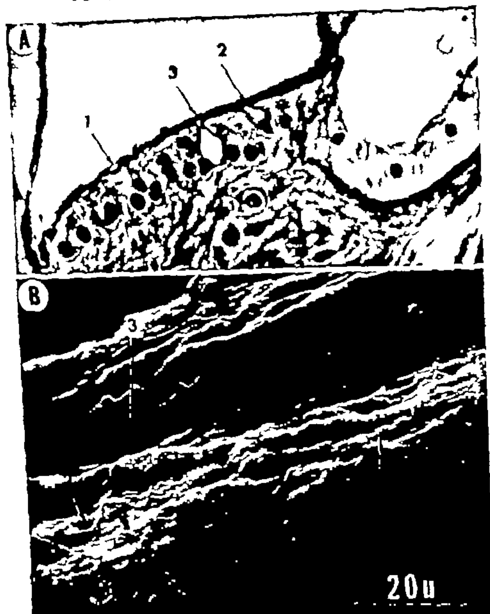


Fig. 8. (A) A phase contrast photomicrograph illustrates interdental cell craters [illegible] the spiral limbus. The different depths of the craters are numbered. (B) A scanning micrograph showing the different depths of the interdental cells craters (numbered) [illegible] the spiral limbus. The cell margin of the interdental cells can be observed.

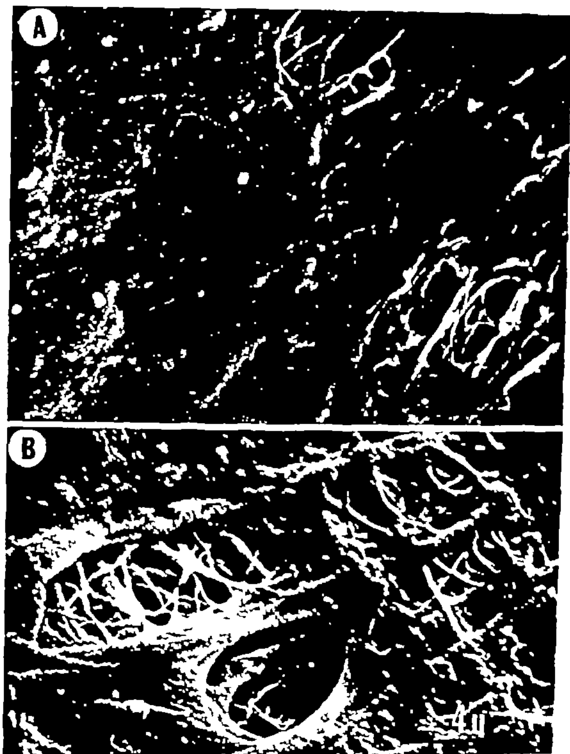


Fig. 7. (A) The epithelial lining of the scala vestibuli showing indistinct cell margins. There are some areas not covered by epithelial cells thereby exposing the underlying spiral ligament. (B) High magnification micrograph of the spiral ligament which is observed in scala tympani.

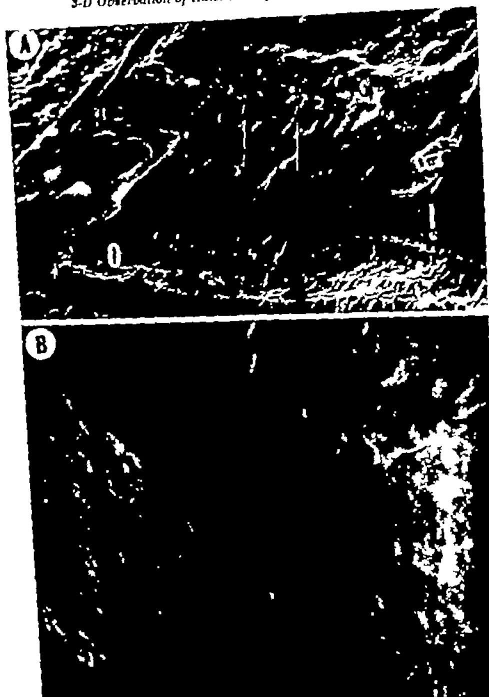


Fig 10 A. A ... micrograph of the orga... of Corti showing ... rea of w ll rranged craters located parallel t the arrangement of inner hair cell (I) Thi... rea coincides with the ... rea of haben la *perforata* nd ... lso with the general ... rea of Hensen stripe of the tectori l membrane when placed on the top of the organ of Corti. O Outer hai cells. B Simila craters (rrow) re seen i ... nother nimal. *IHC*, Inner hai cells. *OHC*, Outer hair cell



Fig 9 An electron microscopi picture h wi g deep Interd ntal cell crat r (I C.) Thi crat Is formed I y the urro ding interdent l cell I t occ l nally it can be f d in a ingl cell Microvilli cover th cell rf ce The ostium f the crat r to se l medi l obstructed by morpho m t ri l in thi c se An rrow i dicates cell ju cti n uggest ing that the crat can be f rmed by m re than ne cell

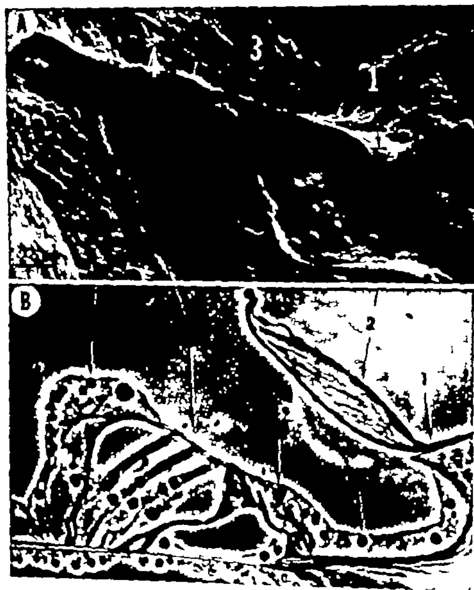


Fig. 14. (*A*, *B*) A scanni g photomicrograph nd phase contrast micrograph re shown for correlation. 1 Spiral limbus; 2, tectorial membrane; 3 inner sulcus cells; 4 inne hair cells; 5, outer hai cell ; 6 Hensen cells.

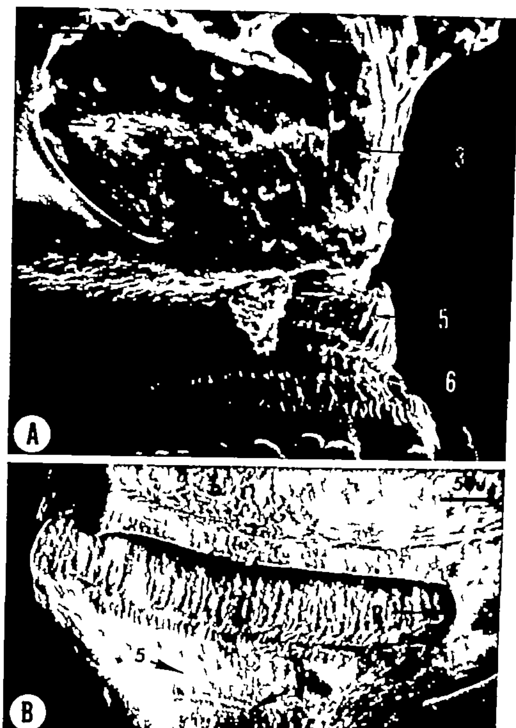
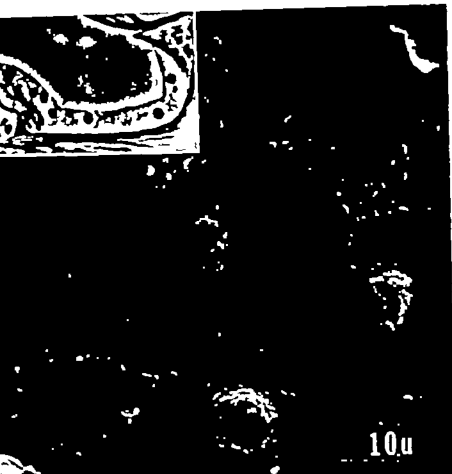


Fig 13 (A, B) Survey scanni g micrographs of th cochlea indic ti g piral limb s (1) tect rial membrane (2) i lcus cell (3) tect rial m mbrane att chm t to th bord r cell (4) i ne h i cell (5) d o te hair cell (6)



ig. 18 A scanni g photomicrograph showi g the inner sulcus cells which ha their urfaces cov red with bundant microvilli. The round protrusions re the uclei of these ells. The insert i phase contrast micrograph showi g the same rea.



Fig. 17 (A) A scanning photomicrograph showing grape-like lipid granules of the Hensen's cells. (B) A phase contrast micrograph illustrating the general relationship between the lipid granules of the Hensen cells (arrows) and the sensory cells. *OHC* Outer hair cells *IHC* Inner hair cells.



Fig. 18. A scanning photomicrograph showing the inner sulcus cells which have their surfaces covered with abundant microvilli. The round protrusions are the nuclei of these cells. The insert is a phase contrast micrograph showing the same area.



Fig 19 (A) A sca nl g phot micrograph of th m llnated ers fibers bserved near th habenula perf rata The m elin sheath resemble a bundle of m c ronl The i c d llcat co tent of th rs fiber probably h hru k d ri g th d l g proce l ing n mpt center portl n. (B) A lectro micrograph f the my li ted ners fibers from the sam re

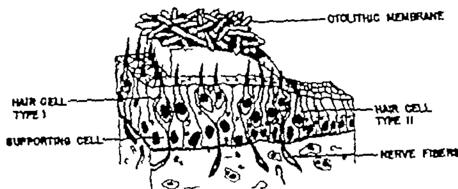


Fig. 20. A schematic drawing of the macula illustrating the relationship between the otolithic membrane and the sensory epithelium. (The drawing is modified from I rato, 1967 Submicroscopic Structure of the Inner Ear. Pergamon Press, London. Drawn by B. Eiter after A. Bertelsen.)

The three rows of hairs of the outer sensory cells were arranged in a "V" shape (Fig. 15 A and B). The hairs of the inner sensory cell were oriented in the same way as the out r hair cells but the "V" was less sharp. The head plate of the inner pillar and phalangeal process of the outer pillar were also identified and are shown in Fig. 16. A definite fibrillar arrangement was observed. The phalangeal processes of the Deiters cells showed irregular urfaces. Hensen s cells always seemed to be dried out leaving distinct grape-like lipid granules in their cytoplasm (Fig. 17 A and B). The cell boundaries of inner sulcus cells were not very distinct but the cell surface possessed abundant microvilli (Fig. 18).

Myelinated nerve fibers

Myelinated nerve fibers located in the osseous spiral lamina were frequently observed in specimens where thi structure had been fractured accident ll . The myelinated nerve fibers appeared like macaroni with the cent r space empty (Fig. 19). Thi appearance wa presumably a result of th drying and hrinking effect on delicat n ural tissue while the tough m lin heath were preserved.

B. Vestibular Organs

Sa cul nd utricle (Fig. 20)

Ma roscopi ally the saccule resembled the shape of an "L" and the utri l resembled an opened shell. The n w drift line of Engström (Johnsson and Hawkins, 1967 b) could be observed in both the utricle and sac le. The long a l of the otoconia varied between 0.5 micron and 17.0 m r ons. The ot conia appeared cylindrical with both end harply angu



Fig 10 (A) A sc nning photomicrograph f the myelinated nerve fiber bserved ne the habenul perf rata. Th m ll sheath resemble a bundl f m caroni The i r d ll ate contents f th nerv fiber probably have shru k d ri g the dri g proce l i g n mpty center porti n (B) An electron mi rograph f the m linated nerve fibers from the sam re



Fig. 22. The sca ning photomicrograph shows the otoconia embedded i the gelatino subst nce

lated The cylindrical portion f some otoconia were also slightly angulated but the angulation was not continu us over the entire body of the otoconia (Fig. 21 A nd B) The surfaces of most f the crystals were smooth but in some cases they were covered with a gelatin like substance (Fig. 22) Occasion lly a band lik structure was seen on the side of the cylinder but this pr bably wa another artifact (Fig. 21 C) Our data sug gests that those cryst l are partially or totally embedded in gelatin

Th distribution of different sizes of cryst ls could not be distinguished with certainty from our material but the finer cryst ls seemed to be located on the surface and peripheral margins of the otolithic membrane whereas the larger crystals were situated in the deep center portion of the mem brane (Figs. 23 A and B, 24 A and B)



Fig 21 (A) A scan i g photomicrograph f th toco from th utri l showing the iz difference between the small nd l rg cryst ls. Observ the cylindrical f rm of th l t ral u f ce f the otoco ia (B) One of th cry t l sh wing t pical cylind ical f rm. (C) Occa l ll d bl band can be observed lt ld (rrow)



F g 22. The scanning photomicrograph show the otoconi embedded i the g l tinous substance

lated. The cylindrical portion of some otoconia were also slightly angulated, but the angulation was not continuous over the entire body of the otoconi (Fig. 21 A and B) The surfaces of most of the crystals were smooth but in some cases they were covered with a gelatin like substance (Fig. 22) Occasionally a band-like structure was seen on the side of the cylinder but this probably was another artifact (Fig. 21 C) Our data suggests that those crystals are partially or totally embedded in gelatin

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Fig. 21 (A) A sc n ng ph t m cr graph f the toco l from th tel l h w ng the l difference between th m ll d l rg rs t ls. Ol serv th cyl d ical f rm of the lateral u face f the ot co (B) On f the crystal sh w g t pical l ndrical f rm. (C) Occa l ll d bl land can be bserved ll d (crow



Fig. 22. The scanning phot micrograph shows the otoconia embedded in the gelatinous substance

lated The cylindrical portion of some otoconia were also slightly angulated, but the ang lation was not continuous over the entire body of the otoconia (Fig. 21 A and B) The surfaces of most of the crystals were smooth but in some cases they were covered with a gelatin like substance (Fig. 22) Occasionally a band-like structure was seen on the side of the cyli d but this probably was another artifact (Fig. 21 C) Our data sug gests that those crystals are partially or tot lly embedded in gelatin.

The distribution of different izes of crystals could not be distinguished with certainty from our material but the finer crystals seemed to be located on the surface and peripheral margins of the otolithic membrane whereas the larger crystals were sit ated in the deep center portion of the mem bran (Figs. 23 A and B, 24 A and B)

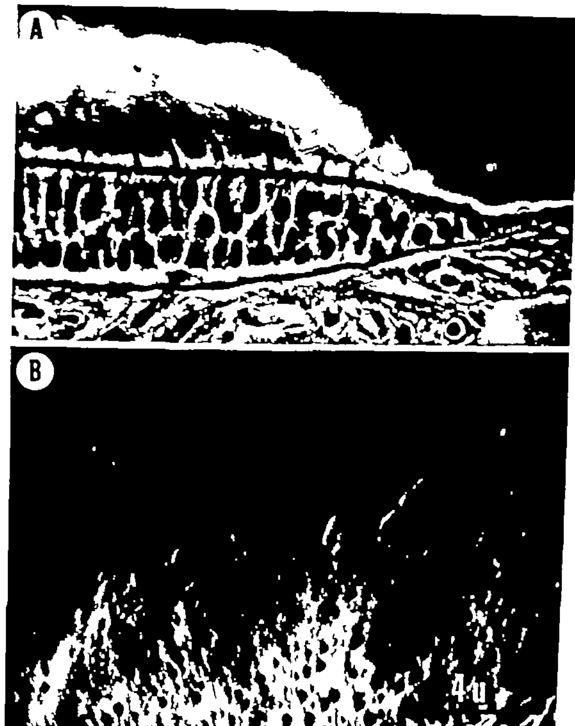


Fig 3. (A) A ph se contra t micrograph of th saccul ill trating the rel ti hip between otoco ia and the sensory epithelium (B) A sc n ing photomicrograph f th saccule howing th m rgin f the t lithi m mbra The adj ce t upporti g cell ne r th m rgi sh w rreg l rf ce



Fig. 24. (A) A phase contrast micrograph of the striola illustrating the relationship between otoconia and the sensory epithelium. (B) The same area as A, viewed by SEM. The snow drift line of Engström is clearly seen. The distribution of the different sizes of the otoconia can be observed. The marginal epithelium near the otolithic membrane appears smooth.

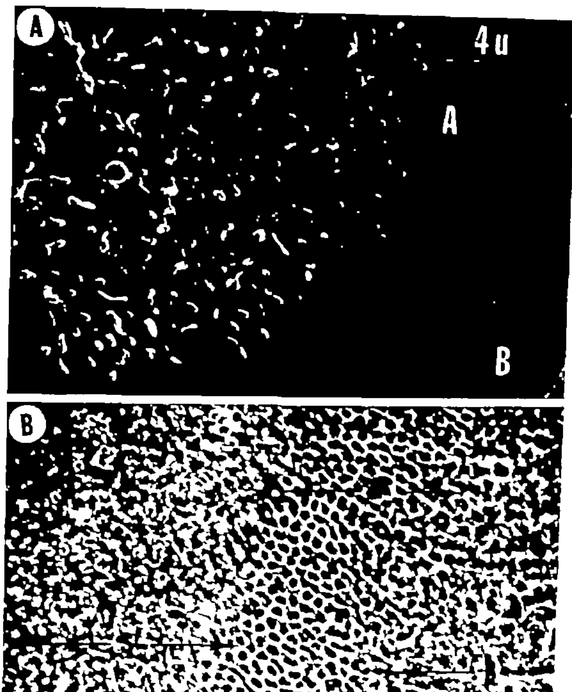


Fig. 25 (A) A surve scan l g micrograph of the utricle howl g abundant b ndles f se sory-cell hairs (S) Th otolithi membrane was digested with cid The epithelial cells nearest t th margin (A) of th sensory epithell m were maller than th t f th dist nt area (B) (B) A phase co trast micrograph f the same rea S Sensory epi thelium A epith lium n rest t the margin of the sensory epith lium B epith lium furthe t from the sensory cell epith li m.

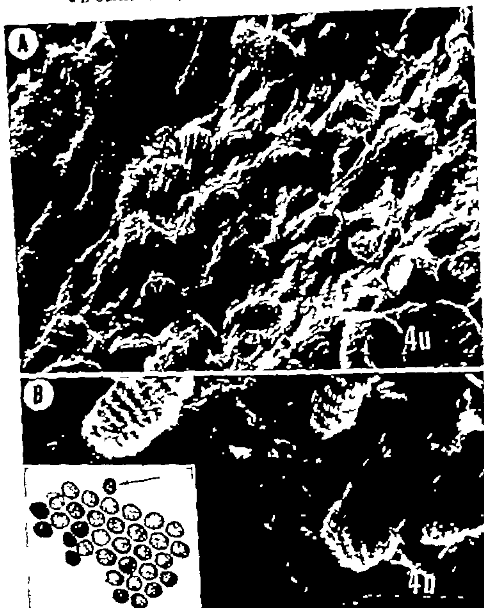


Fig. 36. (A) A scanning photomicrograph f sensory hair f the utricle illustrating their arrangement. (B) A higher magnification f few bundles f sensory hairs showing "church pipe-orga arrangement. The insert is an lectron microscopic photograph of the same area. The arrow indicates the kinocilium. Background crystal are artifacts resulting from the acid digestion.

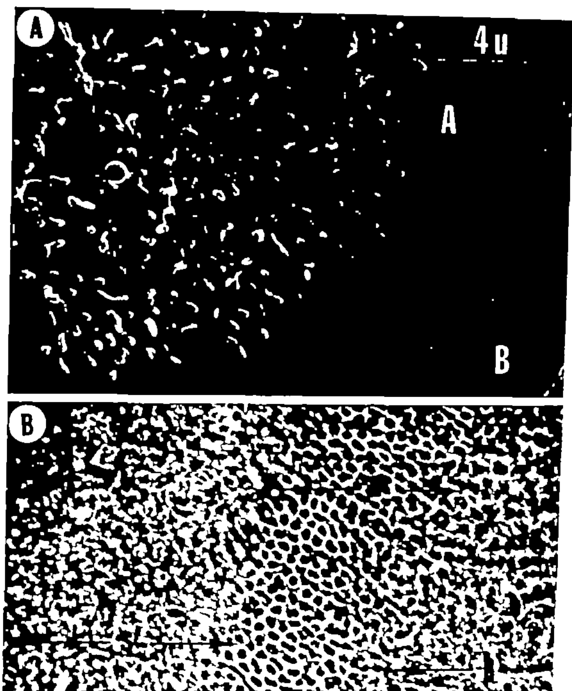


Fig 23 (A) A survey scan ing micrograph of th utricle showing abu dant bundles of sensory-cell hairs (*S*) Th otolithic membrane wa digested with acid The epith lial cell nearest t th margin (*A*) f th sensory epith lium were smaller than that f th dista t rea (*B*) (B) A phase co trast micrograph of the sam area. *S* Sensory epi thelium *A* epithell m earest t the margin f th sensory epithell m *B* epithelium farthest from th se sory cell epithelium

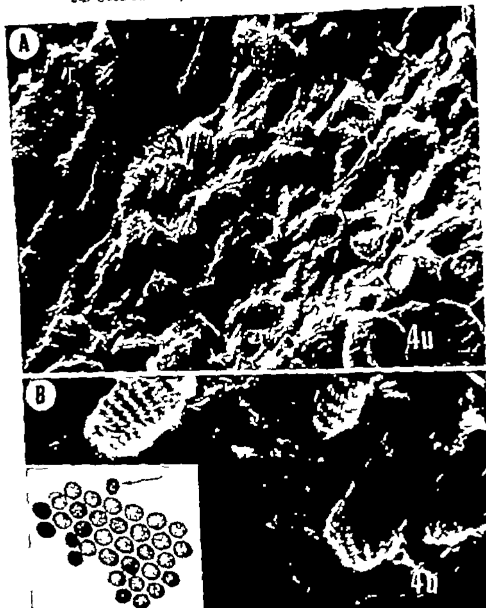


Fig. 26. (A) A *scanning photomicrograph* of sensory hair f the utricl illustrating their arrangement. (B) A higher magnification of *few bundles* f sensory hairs showing "church pipe-orga arrangement. The insert is an electron microscopic *photograph* f the same area. The arrow indicates the kinocilium. Background crystals are artifacts resulting from the *acid digestion*.

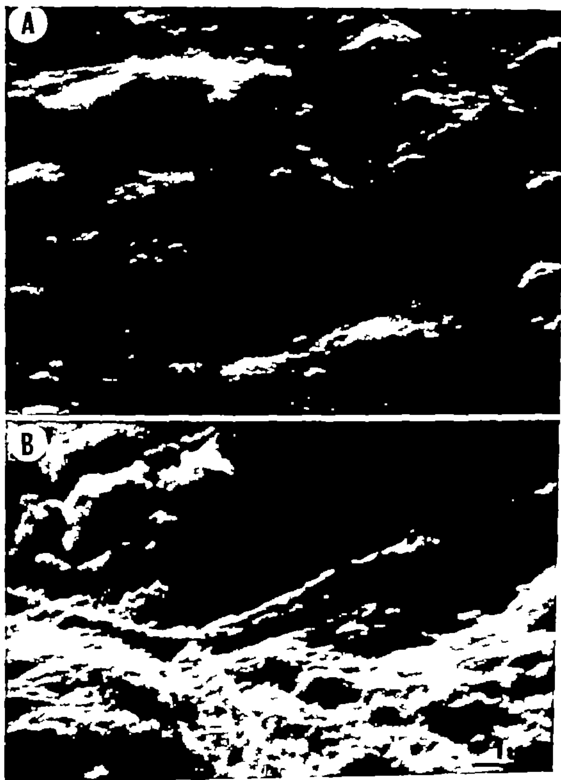


Fig. 27 (A) A sca ing ph t micrograph f the wall ea th se sory area showing f int cellula margi s. Som f th protru i ns re possibl nu l i of the cells. (B) A cell ju ction f the som area Fig A ill strati g a d ubl membran

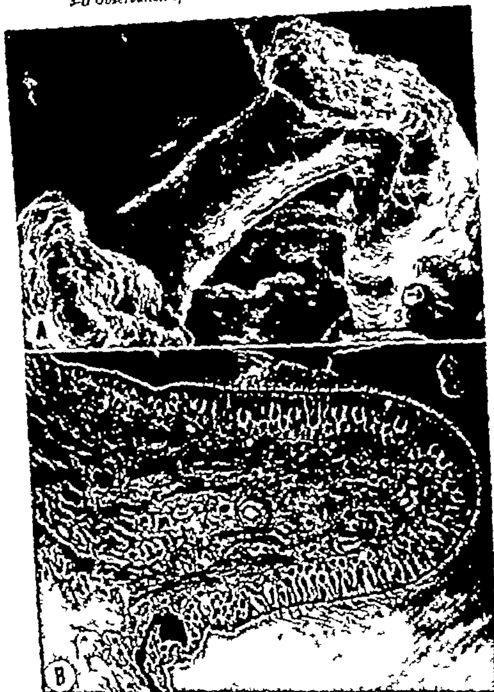


Fig. 28 (*A*) A survey micrograph of the *crista ampullaris* which resembles a saddle. Both ends of the saddle where the pin was small suture is located, are shrunken; artifact. The sensory epithelium was not clearly demonstrated because of the strong vibrations of the gelatinous substance. (*B*) A phase contrast micrograph of the *crista ampullaris* for comparison.

When the otolithic membrane was removed the hairs of the sensory cells were exposed showing the typical hair arrangement of vestibular sensory cells (Fig. 25 A and B) Six or seven rows of hairs graduated in length and caliber resembling organ pipes were observed on a sensory cell Each row contained 10 to 11 hairs. The hair cell arrangements definitely were directional (Fig. 26 A and B)

The supporting cells found between the sensory cells showed rather rough surfaces probably due to abundant microvilli These supporting cells adjacent to the sensory epithelium covered by otolithic membrane were hexagonal They possessed a rough cytoplasmic membrane as a result of a protrusion of cytoplasmic inclusions and nuclei (Fig. 27 A and B)

Crista ampullaris

Technical problems in the preparation of the specimens prohibited the observation of the arrangement of the hairs of sensory cells The planum semilunatum was outlined by hexagonal cells containing numerous cytoplasmic inclusions. The neural epithelium gives the appearance of a saddle (Fig 28 A and B)

DISCUSSION

Submerged interdental cells were first described by Voldrich (1967) who demonstrated the secretory activities of these cells. The observations of the similar structures to those described by Voldrich was also made by the authors using phase contrast and electron microscopy His report concerning the distribution of these submerged cells agrees with our observation that those cells are more commonly found in the apical turn than in the lower turn This finding was supposedly made in the normal guinea pig limbus area Electron microscopic examination clearly shows that this dilated space is lined by the cell membrane of one or two interdental cells and that the cell surface is studded with microvilli Various stages of crater formation were seen suggesting that we were observing the cells in several different physiological states In another study by one of the authors (Lim) which dealt with the enzyme DPNH-diaphorase different states of the enzyme activities in those cells also were demonstrated In the most advanced form the interdental cell resembled a goblet with the narrow ostium opening into the endolymphatic space Occasionally a small amount of residue of a tectorial membrane-like-substance clogged the ostium Scanning electron microscopy verified the above observation suggesting the possibility of free communication of endolymph between this space in the interdental cells and outer scala media The physiologic meaning of this structure is not yet clearly understood although, it is quite reasonable to assume that this structure is concerned with fluid dynamics of endolymph

The less clearly defined cellular arrangement of epithelial cells lining the

scala vestibuli adjacent to Reissner's membrane insertion was in contrast with the well arranged epithelium of the cochlea. The DPNH-diaphorase study mentioned earlier always indicated high enzyme activity in the scala vestibuli suggesting an active participation in energy transport which may be related to the fluid dynamics. Together with Borghesan's "vasculo-epithelial zone" (1957 and 1967) of the limbus near the attachment of Reissner's membrane, these irregularly arranged epithelial cells seem to support the hypothesis that this area could participate in the metabolic process between blood and endolymph.

Our finding of the fibrous arrangement of the tectorial membrane with the radial fibers arranged at about 30–40 degree angle slanting towards the apex of the cochlea agrees with the previous observations made by Hilding (1953) and Iurato (1967). The marginal portion of the outer tectorial membrane gives the appearance of a thickened band and agrees with previous electron microscopic observations of the cut section. This structure may be comparable to that described by Kolmer (1927), de Vries (1949) and others as "Randfasernetz".

Occasionally we observed a wrinkled appearance of the tectorial membrane. The wrinkling effect added difficulty in interpreting the fiber arrangement in this area, but it suggests that these fibers are arranged longitudinally. The wrinkling of the tectorial membrane occurred only at the points of contact with other structures, the limbus spiralis, the area between the outer sulcus cells and the border cells, and the Hensen's cells. Originally we interpreted the wrinkles as an artifact, but in view of the close correspondence of the wrinkles with the points of contact of the tectorial membrane, these wrinkles may have anatomic significance.

The scanning electron microscopic examination revealed a distinct network of fibers on the upper surface of the tectorial membrane which might serve as a net holding the tectorial membrane intact.

The crystalline structure of the otoconia of the utricle and saccule was studied with the greatest interest. Carlström and Engström (1955) reported that these crystals are calcium carbonate in the form of calcite in mammals, birds and sharks, whereas, in amphibia and bony fish they consist of calcium carbonate in the form of aragonite and in the lamprey the crystals are calcium phosphate. More recently Iurato and de Petris (1967) constructed after studying the rat ear a paper model of an otolith based on the cleavage plane of calcite. According to them, the major axis of the crystal forms a hexagonal prism and its side shows clear angulation. In our material the long sides of the prism were not necessarily angulated but rather the crystals resembled a cylinder with both ends having sharp pointed surfaces. This finding was rather consistant in all of our material. The dynamics of the crystals of the otoconia will be discussed in detail in a separate paper (Lim and Lane). Our material indicated that the larger otoconia were in the deep center portion of the neural epithelium whereas, the smaller ones seemed to cover the outer surface and peripheral portion

When the otolithic membrane was removed the hairs of the sensory cells were exposed showing the typical hair arrangement of vestibular sensory cells (Fig 25 A and B) Six or seven rows of hairs graduated in length and caliber resembling organ pipes were observed on a sensory cell Each row contained 10 to 11 hairs The hair cell arrangements definitely were directional (Fig. 26 A and B)

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DISCUSSION

Submerged interdental cells were first described by Voldrich (1967) who demonstrated the secretory activities of these cells. The observations of the similar structures to those described by Voldrich was also made by the authors using phase contrast and electron microscopy His report concerning the distribution of these submerged cells" agrees with our observation that those cells are more commonly found in the apical turn than in the lower turn This finding was supposedly made in the normal guinea pig limbus area Electron microscopic examination clearly shows that this dilated space is lined by the cell membrane of one or two interdental cells and that the cell surface is studded with microvilli Various stages of crater formation were seen suggesting that we were observing the cells in several different physiological states. In another study by one of the authors (Lim) which dealt with the enzyme DPNH-diaphorase, different states of the enzyme activities in those cells also were demonstrated In the most advanced form the interdental cell resembled a goblet with the narrow ostium opening into the endolymphatic space Occasionally a small amount of residue of a tectorial membrane like-substance clogged *the ostium* Scanning electron microscopy verified the above observation suggesting the possibility of free communication *of endolymph between this space* in the interdental cells and outer scala media The physiologic meaning of this structure *is not yet clearly understood* although, it is quite reasonable to assume that this structure is concerned with fluid dynamics of endolymph

The less clearly defined cellular arrangement of epithelial cells lining the

ZUSAMMENFASSUNG

Die Oberflächenstruktur des Innenohres wurde mittels eines Raster elektronenmikroskopes mit 20- bis 20 000facher Vergrößerung stereoskopisch untersucht. Die geprüften Bereiche umfassten das Cortische Organ die Membrana tectoria, den Limbus spiralis, die Stria vascularis, das Ligamentum spirale die kochleären Nervenfasern, das vestibuläre Sinnesepithel und die Otokonien

ACKNOWLEDGEMENT

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of the neural epithelium The snow drift lines of Engström" (Johnsson and Hawkins, 1967 *b*) of both utricle and saccule were also observed in our material Our findings favor the hypothesis that the otoconia are embedded in gelatin rather than that the otoconia just makes contact with the surface of the gel as stated by Johnsson and Hawkins (1967 *a* and 1967 *b*) Occasionally a double band was found on the cylindrical side of crystals and this may suggest the level to which the otoconia were embedded in the gelatin

The arrangement of the sensory-cell hairs of the cochlea and vestibule is in close agreement with the phase contrast microscopic and electron microscopic findings It was noted that the shape of the hairs of the inner and outer hair cells resembled a baseball bat with the handle side attached to the cuticular plate The hairs of vestibular sensory organs resembled a church pipeorgan arrangement the longest hair oriented towards the kinocilium The surface of those hairs was smooth and occasionally they were bent It must be mentioned that the removal of the otolithic membrane by means of acid digestion was essential to uncover the surface of the vestibular sensory cells

This study demonstrates that the application of the scanning electron microscope in the examination of the inner ear structure is quite possible The scanning electron microscope provided clear three dimensional information of the inner ear cell structures of higher resolution and greater depths of field than that provided by other currently available microscopes Adding this new perspective of the inner ear structure which is already complicated by various cells in three dimension, we made a start towards a comprehensive gathering of information with greater resolving power Such an evaluation is an important part of any attempt to understand the meaning of the more common two dimensional observation of microstructures of the inner ear However it must be mentioned that the satisfactory preservation of such fragile structures as Reissner s membrane Hensen s and Claudius cells in the organ of Corti, for the SEM technique still remains to be improved The proper interpretation may require years of accumulation of knowledge and continuing efforts in improving the technique and instrumentation

SUMMARY AND CONCLUSION

The surface architecture of the inner ear was studied employing the scanning electron microscope This instrument gives a three dimensional appreciation of a thick membranous structure which could not be studied with phase contrast microscopy Such structures include the stria vascularis, limbus spiralis, otoconia and vestibular sensory epithelium The major problem with this technique is the proper preservation of the fragile membranous structures.

ZUSAMMENFASSUNG

Die Oberflächenstruktur des Innenohres wurde mitt ls eines Raster elektronenmikroskopes mit 20- bis 20 000facher Vergrößerung stereoskopisch untersucht Die geprüften Bereiche umfassten das Cortische Organ die Membrana tectoria, den Limbus spiralis, die Stria vascularis, das Ligamentum *spirale die kochleären Nervenfasern*, das vestibuläre Sinnesepithel und die Otokonien.

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of the neural epithelium The "snow drift lines of *Engström* (Johnsson and Hawkins, 1967 *b*) of both utricle and saccule were also observed in our material Our findings favor the hypothesis that the otoconia are embedded in gelatin rather than that the otoconia just makes contact with the surface of the gel as stated by Johnsson and Hawkins (1967 *a* and 1967 *b*) Occasionally a double band was found on the cylindrical side of crystals and this may suggest the level to which the otoconia were embedded in the gelatin

The arrangement of the sensory-cell hairs of the cochlea and vestibule is in close agreement with the phase contrast microscopic and electron microscopic findings It was noted that the shape of the hairs of the inner and outer hair cells resembled a baseball bat with the handle side attached to the cuticular plate The hairs of vestibular sensory organs resembled a church pipeorgan arrangement the longest hair oriented towards the kinocilium The surface of those hairs was smooth and occasionally they were bent It must be mentioned that the removal of the otolithic membrane by means of acid digestion was essential to uncover the surface of the vestibular sensory cells

This study demonstrates that the application of the scanning electron microscope in the examination of the inner ear structure is quite possible The scanning electron microscope provided clear three dimensional information of the inner ear cell structures of higher resolution and greater depths of field than that provided by other currently available microscopes. Adding this new perspective of the inner ear structure which is already complicated by various cells in three dimension we made a start towards a comprehensive gathering of information with greater resolving power Such an evaluation is an important part of any attempt to understand the meaning of the more common two dimensional observation of microstructures of the inner ear However it must be mentioned that the satisfactory preservation of such fragile structures as Reissner's membrane, Hensen's and Claudius cells in the organ of Corti, for the SEM technique still remains to be improved The proper interpretation may require years of accumulation of knowledge and continuing efforts in improving the technique and instrumentation

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S U P P L E M E N T U M 254

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SUPPLEMENTUM 254

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CONTENTS

The following code of abbreviations will be used throughout to facilitate the frequent use of the anatomical terminology of the vestibular system

C	cochlear nucleus
CN	cochlear nerve
DAS	dorsal acoustic stria
DR	descending vestibular root
DVN	descending (inferior) vestibular nucleus
EF	efferent fibers (cochlear and vestibular)
HCA	horizontal canal ampulla
LVN	lateral vestibular nucleus (Deiters)
MVN	medial vestibular nucleus
NIV	interstitial nucleus of vestibular nerve
OCB	olivo-cochlear bundle (efferent)
PCA	posterior canal ampulla
RB	restiform body
S	saccule
SCA	superior canal ampulla
SN	saccular nerve
SVN	superior vestibular nucleus
U	utricle
UG	utricular ganglion
UN	utricular nerve
V	descending trigeminal root
VF	vestibular efferent fibers
VII	facial nerve
VN	vestibular nerve
VR	vestibular root
Y	group Y nucleus of Brodal

INTRODUCTION

Anatomical data on the course and central termination of primary vestibular neurons from specific endorgans are essential for the proper design and interpretation of electrophysiological investigation of this neuron. The purpose of this study is to provide such information.

REVIEW OF LITERATURE

The basic manner in which primary vestibular neurons coursed on entering the brainstem was described by early neuroanatomists (Koelliker 1891, Held, 1892, Cajal, 1909). According to these descriptions each vestibular fiber bifurcated within the brainstem into an ascending and a descending branch. The ascending branches supplied the superior vestibular nucleus and part of the lateral vestibular nucleus, while the descending branches comprised the descending vestibular root and gave off collaterals to the descending and medial vestibular nuclei. No correlation of certain fibers with the different vestibular endorgans was given in these or other less extensive reports on the vestibular nerve (Martin, 1894, Sabin, 1897, Winkler, 1909, Sachs and Alvis, 1921, Gray, 1926).

Two later reports have supplied significant information on the central projection of primary vestibular fibers. The first was that of Lorente de Nó (1933) wherein a thorough description was given of the course and termination of various classes (five) of fibers from the cat and mouse labyrinth as depicted by the Golgi method in normal young animals. He suggested that fiber groups I and II, consisting of small and large fibers, respectively represented all the semicircular canals with no differential localization of separate canals. Group IV and possibly Group III projected from the utricular macula while *Group V* represented saccular fibers. Although it is difficult because of nomenclature to identify the precise boundaries of his vestibular nuclei, it is apparent that Lorente de Nó also pointed out that only parts of some vestibular nuclei received primary vestibular afferents (e.g., ventral Deiters). He, however, *did not* include smaller cell groups such as the interstitial nucleus of the vestibular nerve and groups x, y or z of Brodal. His study *represents the earliest* attempt to correlate the innervation of specific vestibular endorgans with different areas of termination in the brainstem.

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A second study of importance was that of Walberg, Bowsher & Brodal (1958). On the basis of central degeneration resulting from complete section of the vestibular nerve via a labyrinthine approach these authors described the manner in which vestibular afferents terminated in the vestibular nuclei. Both the Nauta and Glees silver methods were used after appropriate survival times to allow for wallerian degeneration. They concluded that primary vestibular fibers reach all four vestibular nuclei and cerebellum but that in all of them certain regions were free of vestibular afferents. In the lateral vestibular nucleus, the fibers reached only the rostroventral regions; in the superior nucleus they terminated mainly in the central portion; in the medial nucleus they ended chiefly in the lateral parts; in the descending nucleus all except the rostrolateral region received primary vestibular fibers. They also confirmed the fact that primary afferents terminated in the interstitial nucleus of the vestibular nerve, a point which was made by Cajal (1909) but not mentioned either in a negative or positive way by Lorente de Nó (1933). No attempt was made to identify degeneration from specific endorgans.

A more recent report (Stein & Carpenter, 1967) on the central projection of the vestibular endorgans in the monkey has utilized basically the same method employed in the present study. They demonstrated the central degeneration from lesions in different areas of Scarpa's ganglion which supply the vestibular endorgans. Relatively long (11–14 days) survival times were allowed for wallerian degeneration. No attempt will be made here to review all of their findings but certain projections were startling enough to warrant brief mention. One was the demonstration that the maculae (both utricle and saccule) projected to the superior vestibular nucleus in addition to the medial and descending nuclei. This was in contrast to previous reports and the present one. A second was that separate distinct projections from Scarpa's ganglion centrally could be described for the superior and horizontal canal cristae. A third was that all vestibular endorgans have connections with the interstitial nucleus of the vestibular root. These will be discussed in this report.

It is clear that convincing information on the primary neuron projection from individual vestibular endorgans must be obtained by utilizing the experimental neuronal degeneration techniques. Similar information on the auditory bipolar neuron showing the different localization in the nerve and cochlear nucleus of fibers from different turns of the cochlea, has already been obtained with methods utilizing wallerian degeneration from lesions in the spiral ganglion (Rasmussen *et al.*, 1959) or demonstrating retrograde degeneration from lesions involving the sense organs (Sando, 1965). The reasons for the relative ease of obtaining such data on the auditory neuron are: (1) the surgical accessibility of the cochlea and spiral ganglion in animals for creating lesions in these areas, and (2) the fact that the auditory bipolar neuron will undergo retrograde degeneration regularly after an end organ lesion that is severe enough to injure its dendrite.

Anatomical data on the primary vestibular neuron is more difficult to obtain, because in contrast to the auditory neuron, the vestibular bipolar neuron will not degenerate even following complete surgical destruction of the endorgan. In the present study the data were obtained by creating small lesions in Scarpa s ganglion which lies in the distal portion of the internal auditory canal The resulting wallerian degeneration of the peripheral axon (dendrite) was traced out to the endorgan and correlated with the degeneration of the central axon in the vestibular nuclei. In this way small numbers of primary vestibular neurons can be studied by the experimental neuron degeneration technique

NORMAL ANATOMY AND CONTROL ANIMALS

Certain prerequisite information is essential to this experimental study This includes (1) the detailed anatomy of Scarpa s ganglion and of the vestibular nerve and its branches (2) the limits and architecture of the vestibular nuclei and (3) pattern and distribution in the vestibular nuclei of degeneration from retraction of the cerebellar flocculus necessary for surgical exposure of the internal auditory canal in the cat.

Normal Anatomy of the Vestibular Nerve and Branches

The Sudan Black technique (Rasmussen, 1961) was the method used to tudy the vestibular labyrinth. By this method, the entire nerve supply to the labyrinth enclosed in the petrous bone was stained in toto with Sudan Black B. The myelin sheaths of nerve fibers were colored dark blue. The non nervou tissues (bone and connective tissue) were easily decolorized without destaining the nervous tissue by using graded percentages of ethyl alcohol. The specimen was then decalcified with "Decal requiring approximately 48–72 hours for complete decalcification of the cat petrous bone With the aid of a Zeiss operating microscope the white decalcified bone was then carefully dissected away from the darkly stained nerves to the vestibular endorgans and cochlea using fine forceps on th specimen immersed in 10% formalin The completed dissection revealed the entire membranous labyrinth with all its nerve supply intact.

The author has used thi method to dissect and study the anatomy of the labyrinth f numerous species since 1955 (Rasmussen & Gacek) Approximately 400 normal cat ears have been studied in this manner and thorough familiarity gained of the detailed anatomy of the VIIIth nerve and its branches. Anatomical information was obtained from both intact and sectioned dissected specimens.

1 Careful examinati n f the specimen immersed in a liquid medium (10% formalin) using the dissection microscope was first used to study this anatomy

A Initial examination of the intact specimen revealed the following (*i*) The peripheral vestibular nerve divided into a superior and inferior division Each of these divisions further divided into nerve branches to the five classical vestibular endorgans—*superior division* superior canal crista, horizontal canal crista utricular macula anterosuperior part of saccular macula *inferior division* posterior canal crista saccular macula (*ii*) The vestibular ganglion (Scarpa) which was comprised of cell bodies of the bipolar neurons that make up the vestibular nerve was a very compact, linear arranged cell mass that extended in a rostrocaudal direction It was divided into two more or less distinct masses, the more rostral one being the part associated with the superior division and the more caudal one with the inferior division It was furthermore evident that the ganglion of the superior division was arranged obliquely when viewed from a dorsal aspect its rostral and lying more peripherally in the superior division than its caudal end (the end adjacent to the inferior division ganglion) The cells of the inferior division while remaining compact stretched out caudally over the cochlear nerve trunk as it passed ventral to the vestibular nerve and ganglion (*iii*) Medial to the vestibular ganglion the nerve fibers of both vestibular divisions merged into a single vestibular nerve trunk which entered the brainstem

B The individual nerve branches to each vestibular endorgan were traced back toward the nerve trunk by teasing them out with fine forceps In this way useful information was obtained on the area of Scarpa s ganglion associated with each endorgan (*i*) It was found that the fibers to the macular endorgans were associated with the ventral portions of Scarpa s ganglion The portion supplying the utricular macula occupied the most ventral and caudal region of the superior division ganglion the saccular ganglion was comprised of a mass of cells embedded in the main saccular nerve ventral to the posterior semicircular canal ganglion cells and adjacent to the cochlear nerve trunk The proximal processes of the saccular ganglion were traced in a straight forward course ventral to the cells of the posterior canal fibers to form the most caudal fibers of the vestibular trunk (*ii*) The fibers of the semicircular canal cristae were associated with the dorsal portions of Scarpa s ganglion These to the superior and horizontal canals arose from a cell mass occupying the most rostral portion of the superior ganglion and another one of similar size which comprised the dorso-caudal region of the superior vestibular ganglion this latter mass was positioned directly over the ganglion to the utricular macula By dissection techniques, it was determined that each of the two ampullary nerves (superior and horizontal) was not associated with a distinct portion of the ganglion but that each of these nerve branches received approximately equal innervation from both cell masses concerned with semicircular canal innervation It was as if these were not separate canal innervations but one canal nerve as far as the ganglion was concerned and one which split up peripherally to

innervate two sensory areas. The ganglion cells innervating the posterior canal cristae were those of the inferior division which occupied the most dorsal portion of that mass and which extended caudally over the dorsal surface of th cochlear nerve *The dendrites* of these cells formed the nerve to the posterior semicircular canal crista. The proximal axons of these cells arched rostromedially to join the incoming axons of the superior division canal ganglion cells in the rostral half of the vestibular nerve trunk (*Fig. 45*)

II Examination and reconstruction was done of serial horizontal and transverse sections of the vestibular nerve branches to the labyrinth.

The completely dissected specimens were thoroughly washed with distilled water and then placed in 5% and then 15% gelatin (in 37 C oven) for embedding Under the operating microscope the specimens were oriented in the proper position with a fine needle as the gelatin hardened from cooling with ice cubes. In this way the specimen was embedded so as to obtain either horizontal sections parallel to the nerve fibers or transverse sections *of the* nerve fibers in the vestibular nerve and its branches. These sections were cut on a freezing microtome at 15 μ and serial sections *taken and* mounted in glycerin on slides.

A Reconstruction of horizontal serial sections was utilized to precisely define the location of ganglion cells and their processes The general course of nerves to the vestibular endorgans was confirmed In addition, it was determined that the proximal processes of the utricular *ganglion* cells coursed in a caudo-medial direction *to occupy* a position in the caudal one-third of the vestibular nerve just rostral to the fibers of the saccular nerve (Figs. 14 45)

It was also clearly seen that the axons of the ganglion cells innervating the posterior canal crista swung *rostral to* the utricular axons and joined the axons f the superior division *canals* in the rostral two-thirds of the vestibular nerve trunk (Figs. 14 4 36 *A*) Close examination further clarified *the relationship f ganglion cells to the innervation* of the superior and horizontal canal cristae The dendrites from the rostral cell group of the superior di ision ganglion and those *from* the caudal-dorsal region of the ganglion merged to form *each ampullary* nerve to these canals (Fig. 36 *B*) It also appeared that the rostral *group of fibers* were *of much larger* diameter than those of the caudal groups.

B Transverse sections of the vestibular nerve and branches were informati e on the size and location of *myelinated* nerve fibers.

The most proximal sections *t ken* through the vestibular nerve trunk just distal to the glial-schwann sheath junction showed the rostral portion of the nerve containing fibers from *the three* semicircular canals and a caudal part for fiber from the two maculae (Fig. 1)

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B. Tran verse sections of the vestibular nerve and branches were informa ti e on the ize and location of myelinated nerve fibers.

The most proximal sections taken through the vestibular nerve trunk just distal t the glial-schwann sheath junction showed the rostral portion of the nerve containing fibers from the three semicircular canals and a caudal p rt for fibers from the two maculae (Fig. 1)

A Initial examination of the intact specimen revealed the following (*i*) The *peripheral vestibular nerve divided into a superior and inferior division* Each of these divisions further divided into nerve branches to the five classical vestibular endorgans—*superior division* superior canal crista, *horizontal canal crista* utricular macula anterosuperior part of saccular macula *inferior division* posterior canal crista, saccular macula (*ii*) The vestibular ganglion (Scarpa) which was comprised of cell bodies of the bipolar neurons that make up the vestibular nerve was a very compact, linear arranged cell mass that extended in a rostrocaudal direction It was divided into two more or less distinct masses the more rostral one being the part associated with the superior division and the more caudal one with the inferior division It was furthermore evident that the ganglion of the superior division was arranged obliquely when viewed from a dorsal aspect its rostral and lying more peripherally in the superior division than its caudal end (the end adjacent to the inferior division ganglion) The cells of the inferior division while remaining compact stretched out caudally over the cochlear nerve trunk as it passed ventral to the vestibular nerve and ganglion (*iii*) Medial to the vestibular ganglion, the nerve fibers of both vestibular divisions merged into a single vestibular nerve trunk which entered the brainstem

B The individual nerve branches to each vestibular endorgan were traced back toward the nerve trunk by teasing them out with fine forceps. In this way useful information was obtained on the area of Scarpa s ganglion associated with each endorgan (*i*) It was found that the fibers to the macular endorgans were associated with the ventral portions of Scarpa s ganglion The portion supplying the utricular macula occupied the most ventral and caudal region of the superior division ganglion the saccular ganglion was comprised of a mass of cells embedded in the main saccular nerve ventral to the posterior semicircular canal ganglion cells and adjacent to the coch lear nerve trunk The proximal processes of the saccular ganglion were traced in a straight forward course ventral to the cells of the posterior canal fibers to form the most caudal fibers of the vestibular trunk (*ii*) The fibers of the semicircular canal cristae were associated with the dorsal portions of Scarpa s ganglion Those to the superior and horizontal canals arose from a cell mass occupying the most rostral portion of the superior ganglion and another one of similar size which comprised the dorso-caudal region of the superior vestibular ganglion this latter mass was positioned directly over the ganglion to the utricular macula By dissection techniques, it was determined that each of the two ampullary nerves (superior and horizontal) was not associated with a distinct portion of the ganglion but that each of these nerve branches received approximately equal innervation from both cell masses concerned with semicircular canal innervation It was as if these were not separate canal innervations but one canal nerve as far as the ganglion was concerned and one which split up peripherally to

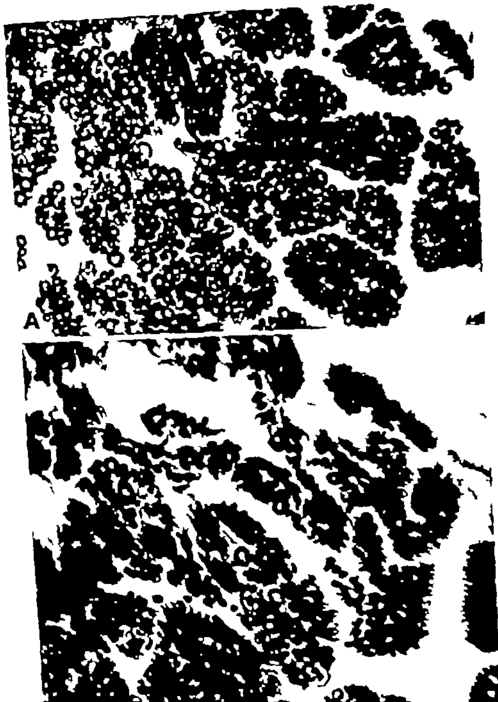


Fig. 3. A High-po er photomicrograph of nerv fibers i the rostral di sion showing the transition bet een smaller fibers t right, t larger at the left. See also Fig. 45. Sudan Black stai the my lin heath. B High-power photomicrograph of nerv fibers i the ca dal division. Not the preponderance of smaller fibers with fewer large ones sca tered throughout

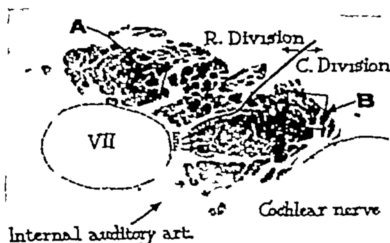


Fig 1 Cross secti n of the vestil ula nerve near the brainstem h wing th rostral (R) and caudal (C) di isions. The f ci l and cochlear nerves and the int rnal udit ry rtery are identified for ori ntati n The squared area indic te locati n of Fig 2, 1 & B. Sudan Black B stain

It was apparent on close examination that the rostroventral part of the semicircular canal portion was occupied mainly by large diameter axons (8–11 μ) while the caudo-dorsal part contained mainly smaller fibers (3–5 μ) (Fig 2 A) proximal to the glial schwann sheath junction the small fibers covered the entire dorsal aspect of the large fiber group As more peripheral sections through the superior division were viewed it was clear that the large axons belong to the rostral group of superior division ganglion cells and the smaller ones to the dorso-caudal group which overlie the utricular ganglion cells at this point (Fig 3) More peripheral sections through the two ampullary nerves of the superior division revealed that the smaller fibers encircled the larger ones until each ampullary nerve has a core of mainly large and a few small fibers and a peripheral zone of almost exclusively very small fibers (Fig 4 A) In terms of destination the core fibers were related to the crest or upper part of a crista while the peripheral fibers innervated the slopes Fiber sizes in the posterior canal nerve displayed the same arrangement with larger fibers in the central portion and smaller fibers in the peripheral zone (Fig 4 B)

Examination of fiber diameters in the caudal division of the vestibular nerve revealed mainly fibers of the smaller diameter group with large ones scattered throughout (Fig 2 B) Fibers from the utricle occupied a rostral and ventral position in the caudal division of the vestibular trunk (Fig 1) As more lateral sections were viewed, the utricular axons passed ventral and rostral to the posterior canal axons to find their cell bodies in Scarpa s ganglion of the superior division These utricular ganglion cells assumed the appearance of a separate ganglionic mass ventral to the cell bodies of the small fibers to the superior and horizontal canal cristae (Fig 3 A) The dendrites of these cells formed the utricular nerv which occupied the



Fig. [illegible] A. Cross section through part of the horizontal canal [illegible] [illegible] g [illegible] small [illegible] fibers [illegible] the periphery [illegible] the [illegible] and larger fibers with some [illegible] the central part of the [illegible] Sudan Black stain. B. Cross section through the posterior canal [illegible] over the cochlear [illegible] (CN) Note the large [illegible] the center of [illegible] surrounded by small axons at the periphery. Protargol [illegible] method.

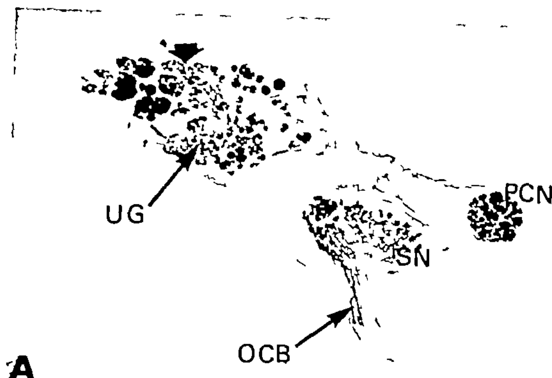


Fig 3 [illegible] through th[e] [illegible] [illegible] division of vestib[ular] n[erve]. Th[e] [illegible] g[an]gl[ion] [illegible] lies [illegible] the [illegible] group of g[an]gli[o]n cell[s] in th[e] upper [illegible] n[illegible] [illegible] indicates the locati[o]n [o]f Fig 3 *B*, [s]h[o]wi[n]g the tra[nsi]tion fro[m] [illegible] nerv[e] fibers c[a]udally [illegible] fibers rostrall[y] in the [su]peri[or] di[visio]n ga[n]gli[on]. O[illegible] ana[illegible] containi[n]g the OCB locates th[e] saccul[ar] nerv[e]. *B*, H[i]gh power ph[ot]omicrograph through the [su]pe[r]ior divi[s]ion ga[n]glion sh[o]wing th[e] d[istributio]n [illegible] of l[a]rg[e] a[n]d [s]mall fiber g[a]ngli[on] cell[s] [s]uppl[yin]g semicircular can[a]l[s]. See [a]lso Fig 45



Fig. 4 A Cros sectio through part of the horizontal canal nerv showi g ery mall nerv f bers at the periphery of the nerv and larger fibers with some maller nes in the central part of the nerv Sud Black stain. *B* Cross section through the posterior canal nerv it rches over the cochlear nerv (CN) Not the large ons in the center of nerv surrounded b small xons t the periphery Protargol sil er method.

ventral and caudal third of the superior vestibular division. The utricular nerve, comprised of mostly small fibers, split off peripheral to the ganglion and bent sharply in a caudal lateral direction to innervate the utricular macula.

Saccular fibers were less numerous than any other vestibular branch (Gacek & Rasmussen 1961) and were also mainly small fibers with some large ones evenly scattered among the smaller ones. In the vestibular nerve they occupied the most caudal and dorsal position (Fig. 1). They coursed in a ventro-lateral direction passing at a right angle to the arching posterior canal axons and ganglion cells, to find the saccular ganglion cells. The ganglionic mass was easily identified by the presence of the vestibulo-cochlear (Oört) anastomosis (Fig. 3 A). The saccular neuron in its entire peripheral course bore a close relationship to the cochlear nerve; its nerve fibers paralleled those of the cochlear nerve.

Anatomy of Vestibular Nuclei

In the older literature much confusion existed because of differences in delineation of the classical vestibular nuclei. The report of Brodal & Pompeiano (1957) has done much to clarify these boundaries and has provided the guideline for the interpretation of degeneration in the brainstem of the cat.

Thionine stained sections of normal cat brainstems and Nauta impregnated experimental brainstem sections which were counterstained with thionine were very helpful in recognizing the various nuclear groups and the morphology of the cells in these nuclei.

A brief review will be presented of the vestibular nuclei, emphasizing features pertinent to the projection of the primary neurons.

Superior Vestibular Nucleus. The SVN was characterized by a population of medium and large neurons which occupied the central portion of the nucleus while the periphery contained small neurons (Fig. 5). These small cells appeared to outnumber the larger ones. Large fascicles of nerve fibers traveled up the central zone in a dorso-medial direction. The cells in the medial part of the nucleus were aligned horizontally in a laminar pattern.

Lateral Vestibular Nucleus. The rostro-ventral part of the LVN adjoined the caudal end of the SVN. The medium sized neurons here were characteristically arranged in rows extending medially from the incoming vestibular root. This arrangement reflected the direction of incoming fiber bundles from the vestibular root to the MVN which was adjacent to the fourth ventricle.

At caudal levels of the LVN a change occurred in the alignment of cells in the ventral division. The medium to large cells here were directed in an oblique dorsomedial direction from the vestibular root. The cells of the MVN at this level also were grouped into a dorsal one lined up with the



Fig. 6. A. Trans erse section through the superior estibula ucleus. Not larger cell bodie i center of nucleus nd mall cells t the periphery Thionine method. B. High-power photomicrograph of 6 A demonstrating the difference i cell size i the SVN.

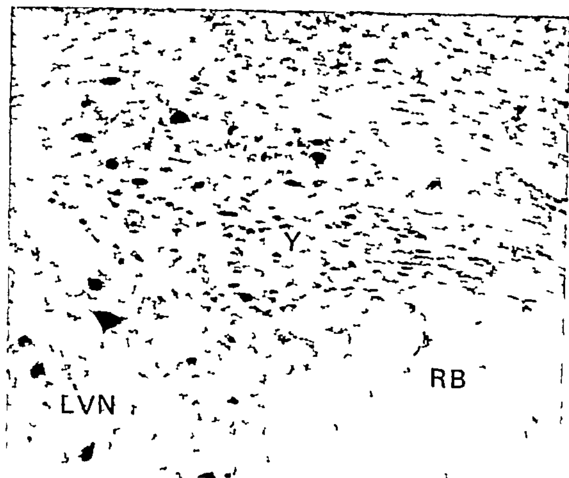


Fig 6 Ph t micrograph f group "y" n leus. Note mostly small and some medium-sized cells in thi nu leus. Thi ine m thod.

cells of the LVN and a ventral one lined up with a lamina of smaller cells probably representing the most rostral limit of the DVN which blended in with the ventral LVN at this level

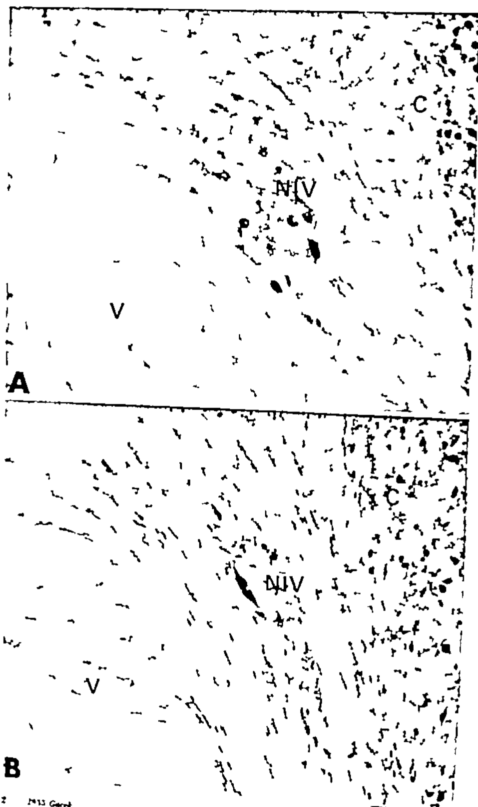
The larger dorsal division of the LVN containing giant multipolar neurons, has been shown by others and by the present study to be devoid of incoming primary vestibular innervation It is not described here

Descending Vestibular Nucleus At the level of the caudal portion of the vestibular root the rostral portion of the DVN became apparent and the ventral LVN was almost gone Just caudal to the vestibular root the laminar arrangement of cells in the rostral DVN was evident Cells belonging to the lateral part of this nucleus were scattered throughout the descending vestibular root no primary vestibular fibers terminated these cells.

In the caudal region of the DVN and the MVN the most striking change

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Fig 7 A Rostral di i io of th I t ralitl l uclea f the estibul n (MV) Thi in method *B* Ca d l di i i n f th MV N t th m ll iz f thi group. Thi ine method.


C
NIV
V
A
C
NIV
V
B

was that the cells were more numerous and diffusely arranged. At this level both cerebellar and primary vestibular fibers ended diffusely in these nuclei.

At these caudal levels the small nucleus labeled group "x" by Brodal was seen (Fig. 6). It was a compact nucleus composed of mainly small cells with a few medium sized neurons scattered throughout the nucleus. This nucleus lay just dorsal to the restiform body and was interposed between the lateral limits of the LVN and medial limits of the dorsal cochlear nucleus; many of the neurons were aligned so that their processes were directed toward the dorsal cochlear nucleus.

The interstitial nucleus of the vestibular nerve was carefully studied in serial sections (Fig. 7). This nucleus was regularly divided into two cell masses, one embedded in the most rostral fibers of the vestibular root and a more caudal one (smaller in size) in the middle portion of the vestibular root. This nucleus was composed of both small and medium sized neurons.

Cerebellar Degeneration from Retraction

It is well known that even the slightest compression of cerebellar or cerebral cortex will produce degeneration of neurons. Axons of these neurons will of course undergo wallerian degeneration and be demonstrated with the technique used here. Several investigators have demonstrated the cerebellar projections from both cortex and cerebellar nuclei onto the vestibular nuclei (Jansen & Brodal 1940, Walberg & Jansen 1961, Walberg *et al.* 1962, Thomas *et al.*, 1956).

In the cat it was decided that the best way to approach the vestibular ganglion for the purpose of making small discrete lesions was through the roof of the internal auditory canal. This required a posterior fossa craniotomy and retraction of the floccular lobe and surrounding cerebellum. The degeneration into the vestibular nuclear complex from this retraction was studied in a control group of six cats.

These six cats were operated upon in exactly the same manner as those experimental ones in which lesions were created in Scarpa's ganglion. The posterior fossa craniotomy was performed and the cerebellum retracted with a malleable metal strip retractor to expose the arcuate eminence and internal auditory meatus. A high speed dental drill was used to remove the roof of the internal auditory canal from the meatus to as far rostral as was possible without damaging the superior petrosal sinus. Bone removal was carried to a point where only a thin shelf of bone covered the internal auditory canal. The shelf was carefully removed piecemeal in an upward direction using small angled ear curettes to avoid damage to the nerves in the canal and also to avoid tearing or tension on the dural lining of the internal auditory canal. The intact dural covering of the vestibular and cochlear nerves was then carefully slit with a small knife and reflected aside to expose the ganglion and nerves of the superior and inferior vestibular divisions, and the cochlear nerve as it passed ventral to the inferior division. No lesion was made, the dural flaps were replaced and the retractor was

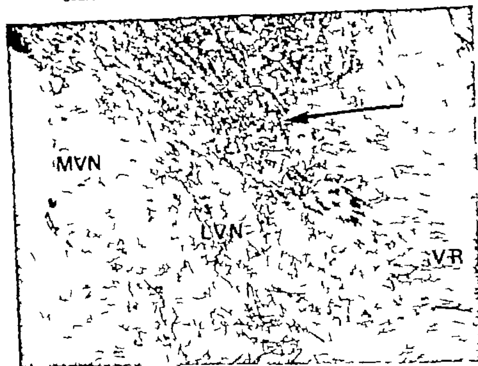


Fig. 8. Tra verse section through the lateral vestibula ucleu (LVN) nd the medial estibul ucleu (MVN) demonstrating the pattern of degeneration (row) from cerebellar retraction. Note the absence of degeneration in entral part of the LVN and MVN w ll incoming estibula root (VR)

removed llowing the cerebellum to re-expand into the cerebello-pontine angl The wound wa closed by approximating two muscle layers over the cranial defect The approximate time for the procedure ranged from 1 to 1 hours.

The six control anim ls were not all operated on at the beginning of the experiment l serie the operation were performed at m re or less regular intervals throughout the period of 2 / years. There did n t appear to be any ignificant decrease in the amount of cerebellar degeneration in the m re recently performed operations. However the amount of degeneration did ary from mild to fairly severe in different animals of this control group The pattern f descending degeneration onto the vestibular complex was con istent

The vestibular area of the brain t m in an animal showing the greatest degree of cerebellar degeneration will be described

Superior Ve tibula Nucleus Although some scattered degenerating fibers were seen distributed in the most dorsal and rostral regions of the SVN most of the degenerating axons in thi area were noted in fascicles descend-

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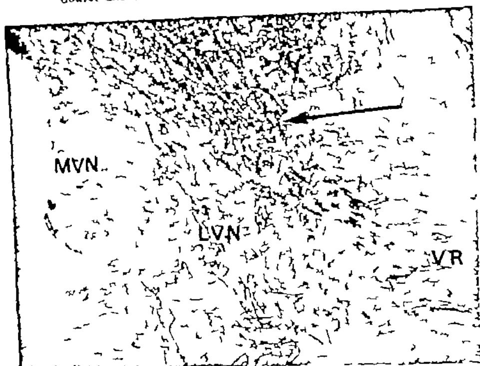


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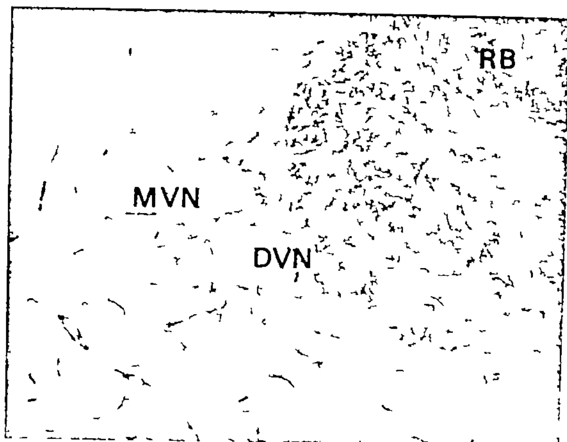


Fig 0 Transverse secti through the caudal half of the MVN a d th DVN Th re are diffuse d generati g cerebellar nerv fibers in thes nuclei

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Lateral Vestibular Nucleus At the junction of the superior and lateral nuclei many descending degenerating fibers were seen in a fascicular arrangement which did not appear to be terminating on cells in the rostroventral extension of the LVN but joined the greatest proportion of all the descending cerebellar degeneratic n to the dorsal division of the LVN (Fig 8) Abundant preterminal degeneration about the cells in this divisi n was seen but none on the cells in the smaller ventral portion of the LVN Some of the descending degeneration continued on in a ventral and caudal direction toward the DVN and the caudal regions of the MVN

Descending (Inferior) Vestibular Nucleus In the rostral part of the DVN where some large and medium sized cells were present occasional preterminal degeneration was seen This region by and large was free of degeneration in even the most severe degree of cerebellar degeneration

However as the more caudal regions of both the DVN and the MVN were

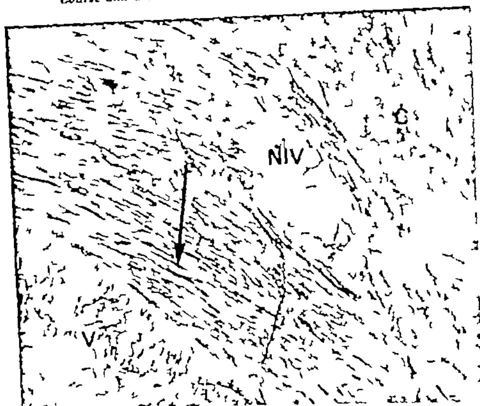


Fig. 10 Vest bula root nd interstitial nucleu in control imal. Note the absence of degeneration i the root nd nucleus. Arrow indicates few ormal fibers which are impregnated with sil er

ex mined, descending deg neration was present scattered throughout the cellular makeup of the nuclei (Fig 9) Abundant preterminal and terminal degeneration was seen Because of the widespread degeneration at these caudal levels, det iled evaluati n of preterminal degeneration from primary afferent destroyed in experimental nim l was not possible

Medial Vestibular Nucela Rostral and midportions of this nucleus were free f degenerating cerebellar axons. However as described in previous sections, the more caudal area of the MVN along with the DVN were con i tently covered with scattered degeneration and could not be precisely evaluated in the experiment l animals.

Oth Nuclei Both divisions of the NIV were consistently free of any degeneration (Fig 10) Since it was of particular importance in the evaluation of experimental results, the small group of cells labeled group "y" by Brodal wa car fully looked for and examined. This group of small cells located between th lateral a pect f the LVN and partly overlying the restiform

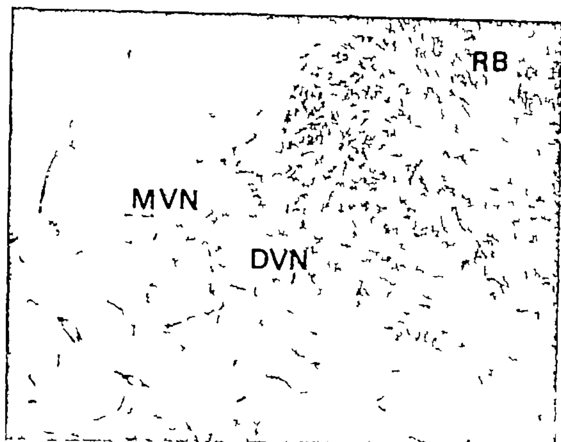


Fig 9 Tran verse section through the caudal half f th MVN a d the DVN Th re are diffuse deg n rating cerebellar nerve fibers in thes nucl i

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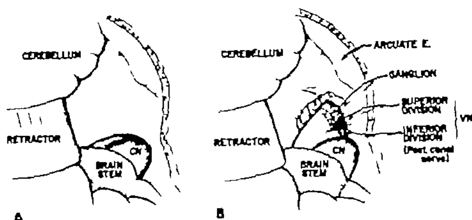


Fig. 12. A Drawi g of the surgical exposure f th internal uditory meal before drilling bon off the petrou segment of the right temporal bone. B, Completed exposur of the estibula er (VN) nd ga glion fter removing the roof of i ternal uditory canal.

ccipital condyles. After slitting the dura over the cerebellum, the arachnoid membranes on the right side were teased away allowing for unrestrained retraction of the cerebellar flocculus and surrounding cerebellar lobe. This retracti n wa effected with a malleable metal strip which was inserted down long the superior urface of the petrous bone from the arcuate emi-nence medially. The flocculus was retracted gently from the subarcuate fossa until the internal audit ry meatus was fully vi ualized with the VIII nerve emerging from it (Fig. 12 A).

The dense bone over the internal auditory canal and medial to the arcuate minence wa then removed with very small cutting burrs until only a thin plate f bon remained covering the nerves in the canal. This final shelf of bone wa rem ved by u ing angled ear curettes and directing th curettage w y from the nerves. The dural covering of the canal was then carefully cut and reflected ide (Fig. 12 B).

Thi xposure allowed vi ualization of the vestibular nerve from its emergence rostro- entral t th cochlear nucleu out to a point 1–2 mm di t l to Scarpa ganglion. The region occupied by the ganglion was indi cated by a narrow pink zone stretching bliquely transverse to the direction f n rv fibers in the uperior divi ion the continuation of this z ne (as the g nglion a sociated with the posteri r canal fibers) could be followed rching caudally ov r the cochlear nerve trunk. The location of the gangli n w accentuated b the lighter appearance of the myelinated axons on eith r id of the ganglion.

Lesions were made only on the right side in each animal with the left n rv and ganglion acting a control. These lesions in various part of the ganglion were made with a (a) mall (0.5 mm) unipolar electrode (2 milliamps for 5 seconds (b) sm ll knife or (c) small needle. The dural



Fig 11 Group " nucl u l n contr l a imal V t th absence f deg erati l thi nu l altho gh there i l und nt d scending cerebell r degenerati n pa l g thro gh the LVN

body was free of terminal degeneration despite the fact it was surrounded by abundant descending degeneration (Fig 11)

Vestibular Root The value of this operative technique for exposing the vestibular ganglion in the internal auditory canal without damaging ves tibular neurons was supported by the absence of degenerating axons in the vestibular root in these control animals (Fig 10)

MATERIALS AND METHODS

Fifty seven healthy y ung adult cats were used in this study N mbutal (30 mg kg) was injected intraperitoneally to effect anesthesia The scalp and posterior cervical skin areas were shaved and prepped surgically after the animal s head was secured in a flexed position with a head holder The usual sterile precautions were adhered to during the operative procedure

A posterior fossa craniotomy was performed carefully removing occipital bone from the occipital crest to the foramen magnum and laterally out to the

The same operation, including exposure of the nerves in the internal uditory canal except for the lesion in the ganglion was performed on six animals. These represented the control animals discussed previously

The remaining 47 cats were processed as described The peripheral lesion with resulting degeneration in the vestibular branches and in the vestibular nerve trunk was reconstructed from the Sudan Black stained sections of the labyrinth. Thi was correlated with the central axonal degeneration in the vestibular root and vestibular nuclear complex.

The Evaluation of Lesions in the Vestibular Ganglion (Scarpa) A crucial part in the evaluation of re ults in this study was the accurate determination f the extent of the lesion in the vestibular ganglion and the resulting degenerati n in the vestibular branches. A short discussion of important factors that could influence this evaluation is appropriate at this point

The primary vestibular neurons are true bipolar neurons whose peripheral processes (dendrites) comprise the nerve branches to the endorgans and whose central processes (axons) make up the vestibular nerve trunk There are over 12,000 cell bodies of these neurons compactly arranged in the vestibular ganglion of the cat A complete evaluation of the lesion includes not only the limits of the injured ganglion cells but also the number and di tribution of the degenerating peripheral processes compared to the number and course of the degenerating central processes produced by the lesion. Thi can only be accomplished by very close examination and reconstruction of th seri l sections of the vestibular nerve and branches. The most useful lesion i a small one limited to the ganglion which produces a number of degenerating fibers peripheral to the ganglion which is approximately *equal* (the number of degenerating axons central to it.

It wa discov red after making several lesion in the ganglion with a small nipol r electrode that, even with little current, spread to surrounding rea wa suffici nt t cause degeneration of axonal processes of cell not in l ed in the intended lesion This was very *misleading in d termining* accurately the vestibular endorgan that was supplied by the group of ganglion cell injured Therefore the electrolytic method of producing small lesions in the ganglion was used *only for very superficial lesions*, and only a fine traight needl or mall knife was used t produce consistently small discrete lesion deep in the ganglionic mass.

It has been pointed out by Rasmussen (1940) and others (Nageotte 1906 Sj'qui t 1928) that wallerian degeneration of nerve fibers distal to the glial-schw nn sheath junction *proceeds* at a much faster rate than central t thi zon Rasmu sen recommended reduction of the survival time in the cat from 10 14 days *down to 5–7 days* for ptimal demonstration of d generated peripheral segment of *nerve fibers*. He admonished that any xperiment l investigati n in dying the demon tration f segments of deg nerating fibers di tal and *proximal t* the glial-schwann sheath zone m t be designed t take into account the differential rates of degeneration

flap was replaced over the internal auditory canal a small piece of gelfoam laid in the bony defect over the canal and the posterior fossa craniotomy defect closed with two layers of muscles. The first layer of deep cervical and temporalis muscles were loosely approximated to allow for expansion of cerebellum from postoperative edema The second layer of superficial cervical and scalp muscles was closely approximated with running chromic suture The skin edges were finally closed with interrupted dermalon suture (000) and plastic spray-on dressing applied

Postoperatively the animals were administered 50 cc of 5% glucose in water subcutaneously but no antibiotics were given to the animals in this series

The animals were observed postoperatively only for gross nystagmus and ataxia with a magnifying lens No attempt was made to record such findings with electronystagmography

The animals were allowed to survive from 4 to 6 days to allow for wallerian degeneration All cats were killed by intracardiac perfusion under general anesthesia according to the method of Koenig Groat & Windle (1945) Three per cent potassium dichromate was added to the 10 formalin perfusion solution in accordance with Rasmussen s modification of the Nauta silver method which was used on the brainstem sections

The animals were then decapitated and the calvarium and bony tentorium carefully removed Dura was reflected over all exposed surfaces of brain and the heads immersed in 400–500 cc of 10 formalin for at least 48 hours before the brainstem and petrous bones were removed This removal was performed under the operating microscope by carefully cutting the emerging cranial nerves of the brainstem without exerting tension on these nerves.

The brainstems and petrous bones were allowed further fixation by immersion for 36–48 hours Brainstems were then trimmed to appropriate size and frozen sections cut at 30 μ The Nauta silver method, as modified by Rasmussen was then *used to demonstrate axonal degeneration in the* brainstem Very close sections were made through the vestibular nuclear areas of each animal and reconstructed to evaluate the degeneration pattern resulting from the various lesions in Scarpa s ganglion

The petrous bones were stained *in toto* with Sudan Black according to Rasmussen s technique The vestibular complex of nerve branches was obtained by carefully dissecting away the decalcified bone under the dissecting microscope as described in the previous *section on normal vestibular* anatomy These specimens were then embedded in 15 gelatin and serial frozen sections cut (15 μ) on a plane parallel to the superior and inferior division fibers In this way degenerating fibers were optimally demonstrated in the nerve branches.

Of the 57 animals operated upon in this experiment four animals died in the first one to two days following surgery Since there was no evidence of infection or hemorrhage it is *possible that increased* intracranial pressure possibly from edema was instrumental as the cause of death

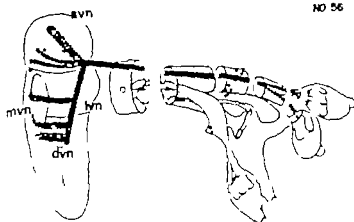


Fig 13. Drawi g of the reconstructed lesion d degeneration pattern i imal 56 See Figs. 4 nd 46 for label t estibular endorgans n the right nd the estibul nei i on the left

cent to the ro tral divi ion of the interstitial nucleus, abundant terminal degenerati n was seen in thi nucleus (Figs. 16, 17) These apparently represent collaterals from the incoming degenerating axons because the number of degenerating fibers n either side of the nucleus appeared equal.

At the dorsal a pect of the descending trigeminal root, these degenerating ax n bifurcated int an ascending and a descendi g branch. The ascending bran hes turned al ruptly in a dorsomedi l direction toward the central region of the SVN (Fig 16) Long collaterals were seen emerging from these ascending branches in the ventral part of the nucleus (Fig. 18) There ppeared t be nly one collateral branch from each ascending fiber These c llat rals were seen swinging in a medial and then d rsal direction to ppr ach medium-sized cells tretching across the medial half of the SVN t ward the f urth entricle The most medial extent of this group of cells ppeared to merge with the rostral end of the MVN Rich preterminal degeneration wa seen around these cells.

Beyond the take-off of collaterals, the ascending xons continued up the cent l region of th SVN in a d rsomedial directi n and terminated on the large nd medium cell in thi p rtion of th nucleus (Fig 19) The smaller celled perip heral zon of the nucleu wa free of degeneration. It was not pos ibl t determine whether these large degenerating ax ns continued up int ll cerebellar area because of the presence f descending cerebellar degenerati n in thi area f the SVN

The descending branches in thi animal were seen as coarse degenerating fibers located in the most medial nd v ntral position in the descending estibul r r ot A these fibers pa sed caudally in the root they could be seen coursing entral t the n rmal incoming primary afferent axons of the vestibular roo t. In the caudal h lf f the ventral divi ion of the LVN

in these two regions. Therefore survival time allowed for wallerian degeneration in this experiment ranged from 4 to 7 days.

The significance of this point was emphasized when lesions were placed in those parts of Scarpa's ganglion that gave rise to the smaller caliber fibers. It is well known that (1) small fibers degenerate faster than large ones and (2) the peripheral process of a bipolar cell is of smaller caliber than the central one. Therefore the distal processes of the ganglion cells in the small fiber population are indeed very small. If an animal with a lesion in this part of the ganglion were allowed to survive 10–14 days, the distal processes of the injured ganglion cells would have completely degenerated and could not be demonstrated histologically with the Sudan Black technique. This obviously would effect the evaluation of the degeneration pattern significantly.

OBSERVATIONS

The lesions and resulting peripheral and central degeneration in *six* animals will be presented in detail to demonstrate the projection from the vestibular endorgans. The results in remaining cats were used to confirm these lesions either by duplicating them exactly or by the inclusion of more than one sensory area's nerve supply. These will not be discussed in detail in this report.

SEMICIRCULAR CANALS

A. *Superior Division* (Superior and horizontal canals)

Cat 0C (Fig. 13). In this animal a very small lesion was made with a straight pick directed into the rostral part of the ganglion of the superior vestibular division on the right. Postoperatively the animal demonstrated a gross horizontal rotatory nystagmus to the left which persisted for 3 days. The animal was perfused 5 days postoperatively.

(*a*) *Lesion and peripheral degeneration*. Reconstruction of the lesion showed a very small area of destruction in the rostral part of Scarpa's ganglion (Fig. 14 A). Degenerated large-sized fibers coursed distally from the lesion and then diverged so that approximately half entered the nerve to the horizontal canal and half to the superior canal nerve. The degenerated fibers occupied a central position in the ampullary nerves (Fig. 15).

A compact bundle of dengerated axons was seen coursing centrally from the lesion in Scarpa's ganglion (Fig. 14 *B*). This bundle was located in the rostral region of the vestibular nerve trunk and remained in this location as the vestibular nerve became the vestibular root in the brainstem.

(*b*) *Central degeneration*. Large degenerating axons were seen coursing in the most rostral part of the vestibular root. As these fibers passed adja

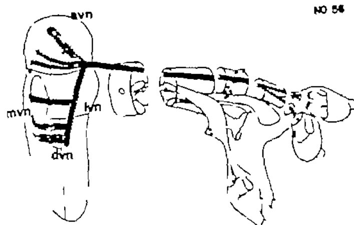


Fig 13 Drawing of the recon tructed lesion and degeneration pattern in im 1 56 See Figs. 45 nd 46 for label t estibal endorga the right nd the estibula nuclei on the left.

cent t the rostral divi ion of the interstitial nucleus, abundant terminal degeneration was seen in this nucleus (Figs. 16, 1) These apparently represent collateral from the incoming degenerating axons because the number of degenerating fibers on either side of the nucleus appeared equal

At the dorsal n peet of the descending trigeminal root, these degenerating x n bifurcated into an ascending and a descending branch. The ascending branches turned al ruptly in a dorsomedial direction toward the central region of the SVN (Fig 16) Long co llaterals were seen emerging from these scending branches in the ventral part f the nucleus (Fig 18) There appeared t be only one collat ral branch from each scending fiber These ollateral were seen winging in medial and then dorsal direction to pproa h medium-sized cell stretching acros the medial half of the SVN tow rd the fourth v ntricl The most medial extent of thi group of cells ppeared to merge with the rostral end of the MVN Rich preterminal de generation was seen round these cells.

Beyond the t ke-off f collaterals the scending axon continued up the entral region of the SVN in a d rs medial directi n and terminated on the l rge and medium cells in thi p rti n of the nucleus (Fig 10) The smaller celled peripheral zon of the nucleus wa free f degeneration. It was not p ible t determine whether these large degenerating axons continued up t th cerebellar area because of the presence of descending cerebellar degenerati n in this rea of the SVN

The descending branches in thi nimal were seen as coarse degenerating fibers l cated in th most medial and ventral position in the descending vestibular root A these fibers pa sed caudally in the root, they could be seen coursing entral to th norm l incoming primary afferent axons f the vestibular root In the caudal half f the ventral divisi n of the LVN

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OBSERVATIONS

The lesions and resulting peripheral and central degeneration in six animals will be presented in detail to demonstrate the projection from the vestibular endorgans. The results in remaining cats were used to confirm these lesions either by duplicating them exactly or by the inclusion of more than one sensory area's nerve supply. These will not be discussed in detail in this report.

SEMICIRCULAR CANALS

A. *Superior Division* (Superior and horizontal canals)

Cat 3C (Fig. 13). In this animal a very small lesion was made with a straight pick directed into the rostral part of the ganglion of the superior vestibular division on the right. Postoperatively the animal demonstrated a gross horizontal rotatory nystagmus to the left which persisted for 3 days. The animal was perfused 5 days postoperatively.

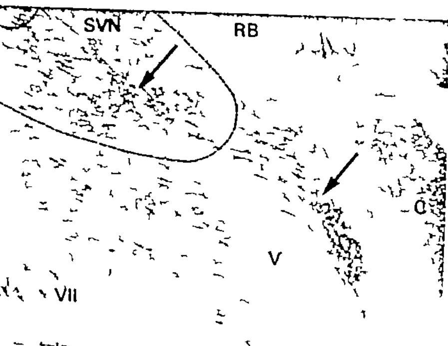
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15. High power phot micrograph f the superior canal erv showi g degenerating ipheral on (rrow) f the ce tral part of the nerv A lm 1 84.



r 1 X preparation of the estibul root nd superior estibular nclens f lmal Not the degeneration I root, I terstitial nclens of root nd conti tion f scond branches in the center of the SVN (arrows Broken line indicates limit of th SVN

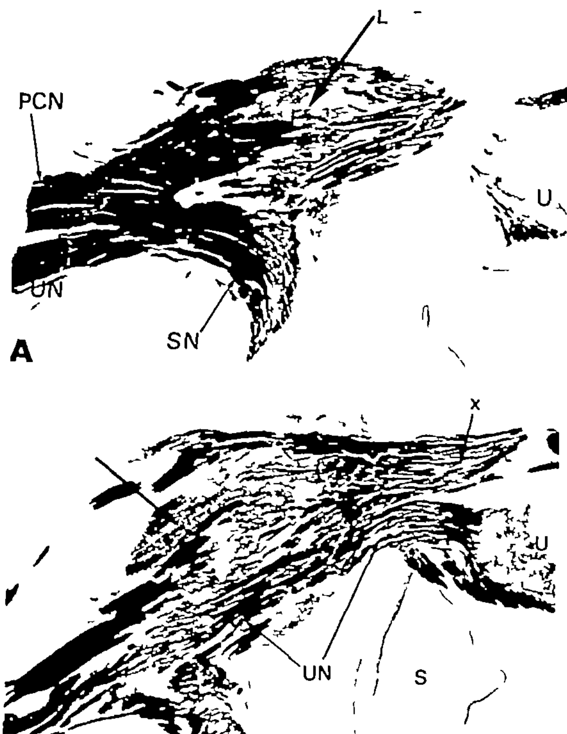


Fig 14 A Lesi n (L) in Sc rp ga gli f n m l 58 Not the posteri nal fibers archi g f rward i to th ro t al l l l f th estib l rs B, Pro im l bu dl f d g nerati g x from tl l lm l 36 l l di ted h the h arr rrow Thi m re tral sect lso h w tl c f th utricul r rs (UN) from d rgan (U) t g gli n nd the est bul ners trunk "x ref rs t the locati f Fig 15 in the upe (l rs

Fig. 15. High power photomicrograph f the superio canal nerv showing degenerating peripheral xons (arrow) i the central part of th nerv A imal 56.

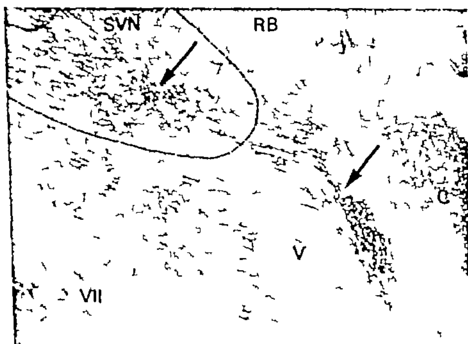


Fig. 16. Sagit preparation f the estibula root nd uperior estibula nucleus i lm l 58. Not the degeneration i root, i terstitial ucleu of root nd continuation of scend ing branches i the center of the SVN arrows). Broken line indicates limit of the SVN

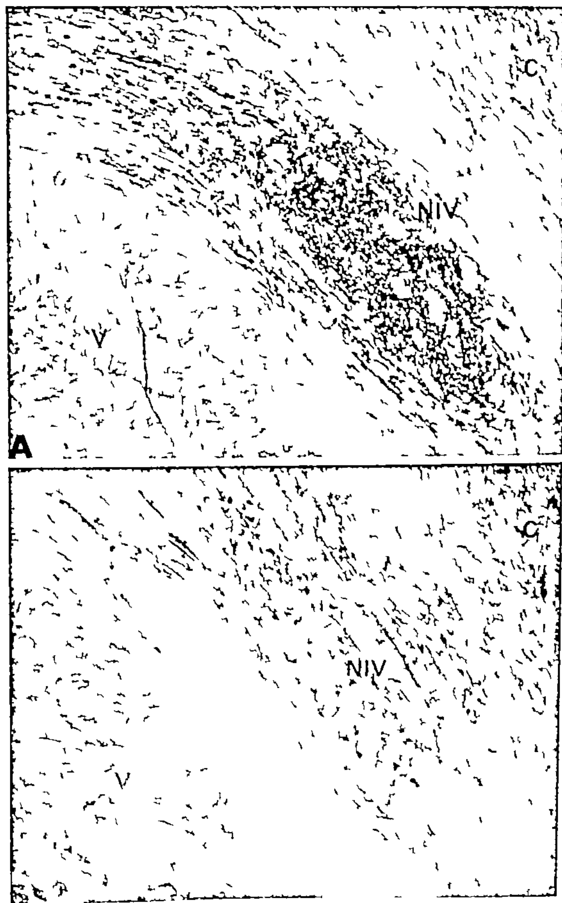


Fig 17 A B High-pow photomicrograph f the vestib la root in Fig 16 sh wi g th bund nt dege rati n i the rostral di i i n f the NIV (A) Th caudal di i i n f the NIV (B) i free f deg n rati n

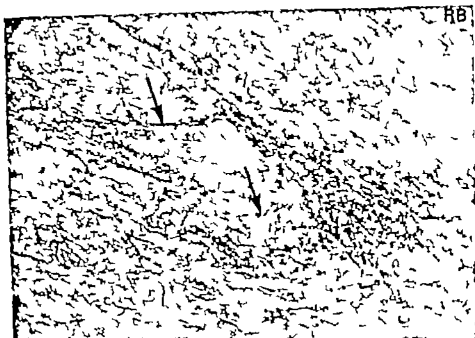


Fig. 18. High-power photomicrograph of the SVN i Fig. 16 showing the medially directed collateral (rrows) lea i g the scending branches f deg nerati g estibul fibers.



Fig 19 More rostral tra erse section through the SVN of ical 84 There is preter minal nd terminal degeneration around the l rger neurons in the center f the nucleus (rrows) hile the peripheral one is clea at pper right.

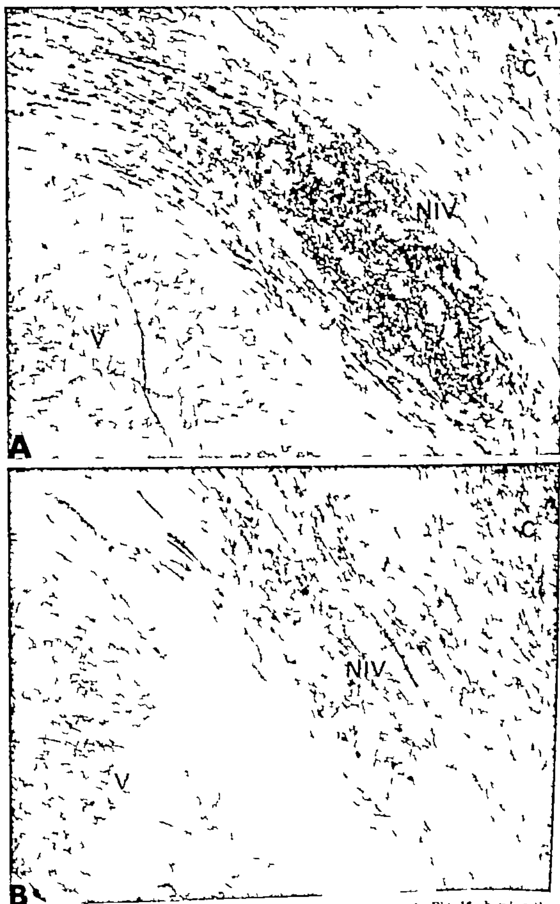


Fig 17 A B High powe ph t micrograph f the vestibul root in Fig 16 h wi g the abund nt deg tion i th rostral divi i n f the NIV (A) Th audal divi i n f the NIV (B) i free f deg nerati n.

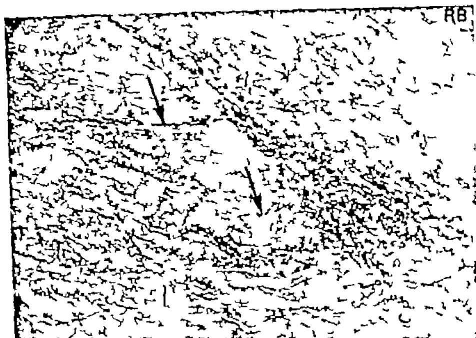


Fig. 18. High-power photomicrograph of the SVN i Fig. 16 showing the medially directed collateral (arrows) leaving the ascending branches of degenerating estibular fibers.



Fig. 19. More rostral transverse section through the SVN of mal 86. There i preter minal nd terminal degeneration around the larger neurons in the center of the nucleus (arrows) bu the peripheral zone lear t upper right.

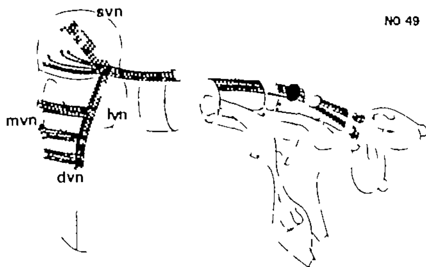


Fig 20 Drawing of th recon tructed lesion and degenerati pattern in nimal 49 The he vy brok n lines represent l rge siz deg n rating fibers.

collaterals could be seen taking off at right angles to these descending root fibers and passing obliquely across the LVN without terminating on any of the large or medium sized cells These collaterals were directed toward the dorsal half of the MVN and were seen to terminate near cells in that part of the MVN and also around medium sized cells at the medial most region of the LVN

As the degenerated descending rami were followed still more caudally in the descending vestibular root and reached levels of the rostral part of the DVN more collaterals were seen to arise and course in a directly medial direction Preterminal degeneration was noted around some small and medium sized cells in the DVN but none around the large cells. Most of the *collaterals passed through the dorsal acoustic stria and terminated in the* ventral portion of the MVN Here preterminal degeneration was seen in the lateral part of the nucleus.

In more caudal regions of the descending vestibular root the degenerating axons became more diffusely arranged among the other normal fiber components of the root and the collaterals travelling medially also were scattered throughout the DVN and MVN From this level caudalwards, it was impossible to determine precise terminations of the vestibular afferents because of the presence of descending cerebellar degeneration into this same area

Cat 49 (Fig 20) It is of interest to note the findings in an animal with a more extensive lesion in the large fiber population In this animal a small knife was used to make a lesion in the rostral one-third to one-half of the superior vestibular ganglion The animal demonstrated a marked horizontal-rotatory nystagmus to the left for 3 to 4 days postoperatively This animal was perfused after 7 days survival time

(*a*) *Lesion and peripheral degeneration* A large lesion was found involv

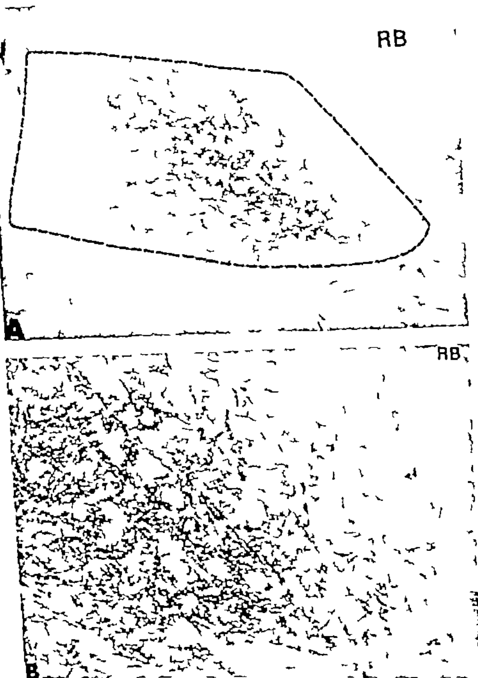


Fig. 31. A, Transverse section through the SVX of animal 49. Note the degeneration limited to the central area of the nucleus despite the large size of the lesion. Broken line indicates limit of the SVX. B, High power photomicrograph of (A) demonstrating the location of degeneration around large neurons in the center of the nucleus. Note the absence of degeneration in the periphery.

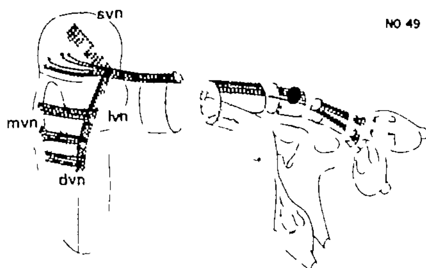


Fig 20 Drawing of the reco truct d lesion and deg nerati n pattern in animal 49 The heavy brok n lines repres nt l rge si e deg nerati g fibers

collaterals could be seen taking off at right angles to these descending root fibers and passing obliquely across the LVN without terminating on any of the large or medium sized cells These collaterals were directed toward the dorsal half of the MVN and were seen to terminate near cells in that part of the MVN and also around medium sized cells at the medial most region of the LVN

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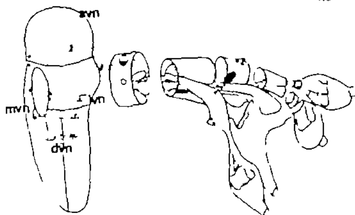


Fig. 23. Drawi g of the reconstructed lesi nd degeneration pattern i nimal 5. The light broken lines represent mall-sized degenerati g fibers.

ing the rostral half of the superior gangli n From this lesion, large caliber degenerated, myelinated fibers passed peripherally toward the nerves of the superior and horizontal canals. The large number of degenerated fibers formed two compact bundles of fibers as they coursed peripheral to the lesion in the ganglion. These became surrounded by a ring of normal small sized, myelinated fibers as they f rmed each ampullary nerve of the superior division.

(*b*) *Central degeneration* Th pattern of the central degeneration from this large lesion was essentially the same as in animal 56 Only the intensity was increased proportionately All the preterminal degeneration in the SVN was localized in the central portion of the nucleus while the periphery was free of degeneration despit the ize of the lesion (Fig. 21) The terminal nd preterminal degeneration from the degenerated large-sized fibers, there fore, appeared localized to the large cells in the central part of the SVN In other areas of the vestibular nuclear complex, the pattern of degeneration remained the same as in animal 56, but intensity of degeneration was in creased (Fig. 22)

Cat 3 (Fig. 23) A uperficial lesion of the caudal half of the superior divi sion ganglion was attempted in this animal By involving only the most dor sal cell in this part of the ganglion the lesion avoided including the deeper cells innervating the utricular macula. It was found that such a superficial lesion could best be mad by barely touching the tip of a small unipolar electrod to the surface of the ganglion and applying 2 milliamps for 5 seconds.

Following surgery the animal had a barely perceptible horizontal nystag

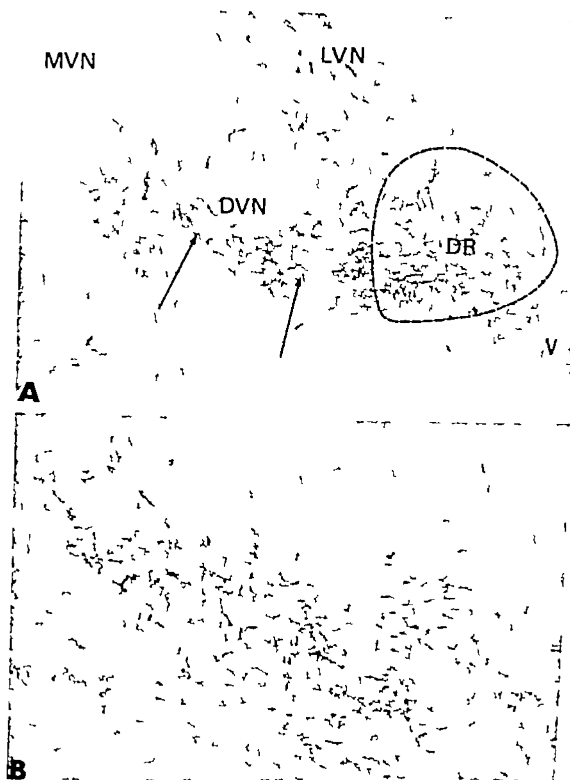


Fig 22. (A tra rse secti through the descending estibul root (i dicated by brok n li) and th ro t I DVN nd MVN I anim 1 49 Th desce di g I anel f th deg ting fibers occup th entral d l teral re f the root d gi ff medi lly directed coll t ral (ws) t th DVN a d MVN B High po w ph t micrograph of th llat ral I (1) N t h w the coll teral by pa th large uro but end medi m ized cell I the DVN Th se coll teral terminat t l rg t t in the MVN t the l ft

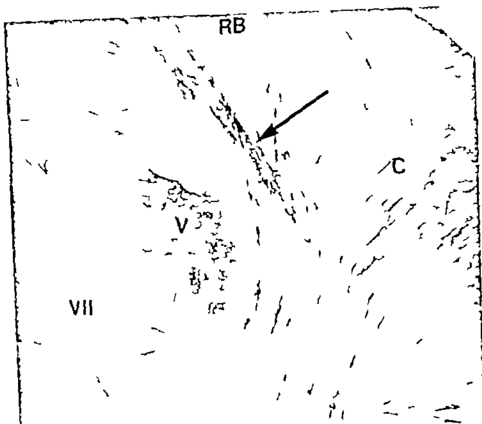


Fig. 23. Transverse brainstem section showing the degenerating small nerve fibers (arrow) located in the lateral aspect of the vestibular root of animal 5.

mus to the left. This was in marked contrast to animals 56 and 49. The animal was sacrificed by perfusion after 5 days.

(*a*) *Lesion and peripheral degeneration.* The lesion successfully destroyed most of the caudal one-third of the superior division ganglion (Fig. 24 *A*). Fine degenerated fibers were seen coursing as a compact bundle to surround and intermix with large normal fibers forming the ampullary nerves.

The central processes of the ganglion cells destroyed by the lesion were followed as degenerated fibers in the dorsal and midportion of the vestibular nerve trunk. Careful reconstruction of the serial sections through this labyrinth confirmed that the lesion did not extend deep enough to involve the utricular ganglion cells which lie directly beneath this part of the superior division ganglion (Fig. 24 *B*). The utricular nerve was normal.

(*b*) *Central degeneration.* The centrally coursing degenerated axons occupied the dorsal part of the rostral two-thirds of the vestibular nerve trunk. This area normally contains smaller caliber fibers.

The degenerating fibers coursed in the lateral part of the incoming vestib-

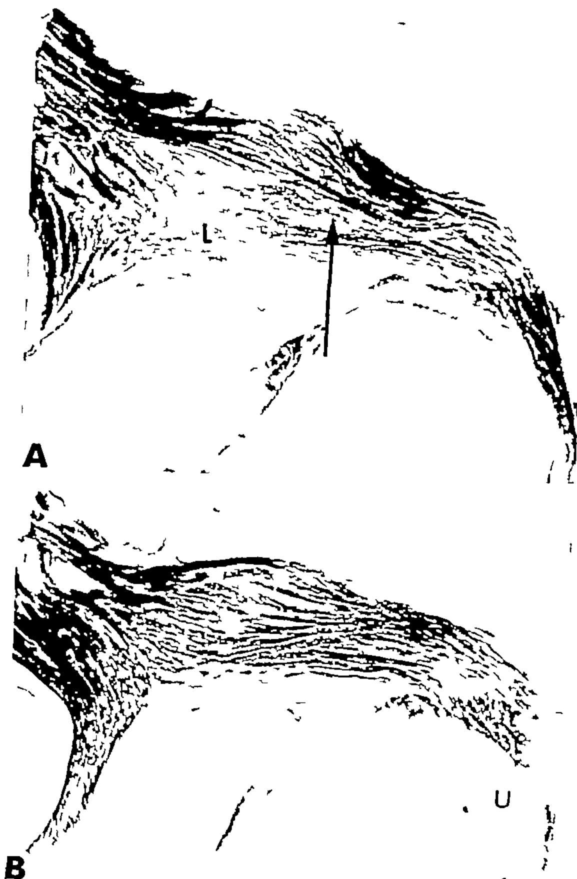


Fig 24 A II rız t I ectI thro gh the d rs I regi f th perıor dI I g glio I nimal 5 The lesI (L) i vol es th a d I pect f tl I ga gll n. Arrow poi t t bu dI f deg rati g ers fibers passi g periph rall B Sam pecim n in (A) but m re e tral secti h wi g n I vol me t f th deepe g gll cell whi h uppl the utricl

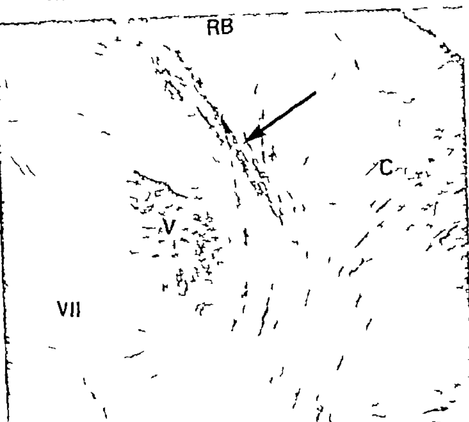


Fig. 25. Transverse brainstem section showing the degenerating small nerve fibers (arrow) located in the lateral part of the vestibular root of animal 5.

mus to the left. This was in marked contrast to animals 56 and 49 The animal was sacrificed by perfusion after 5 days

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The degenerating fibers coursed in the lateral part of the incoming vestib-



Fig 24 *A* H rlz nt l secti thro gh th d rs l regi f th superi dl l i g gli n l lmal 5 The l l n (*L*) involes th c dal pect f thi ga gli Arrow poi t t n b dl of d g rati g nerv fibers pa ing peripherally *B* Sa e pecime a in (*A*) b t m re v tral secti howing no inv lveme t f the deepe g gli n cell whicl supply the utricle

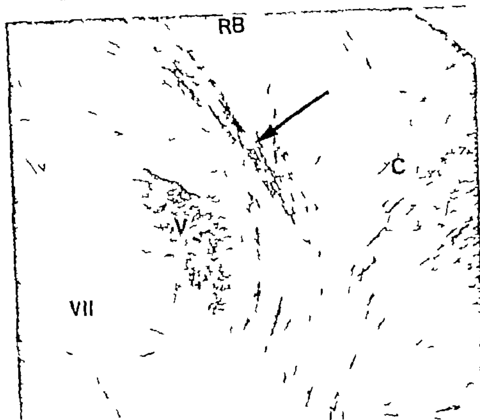


Fig. 23 Transverse brainstem section showi g the deg nerating mall nerv fibers (arrow) located i the lateral pect of the vstibula root f imal 5.

mus to the left This was in marked contrast to animals 56 and 49 The animal was sacrificed by perfusion after 5 days.

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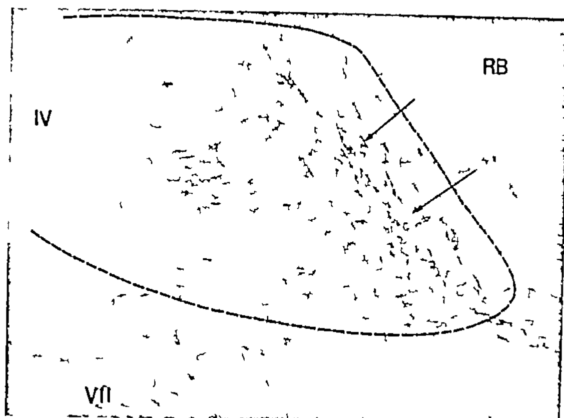


Fig 26 Tran v rse sectio through tl SVN f ni al 5 l m trating th loc tion f ascending bran l es f degene ating mall fibers in th l teral a pect f the nu leu Comp re with Fig 16 and 21 Broken lin lelimits tl SVN

ular root (Fig 25) terminated by means of collaterals on the rostral divi sion of the interstitial nucleus, and finally bifurcated into ascending and descending branches at a more dorsal and lateral point than the larger fibers described in animals 56 and 40

The ascending branches of the small degenerating axons abruptly turned dorsalward and coursed as individual fibers, or packets of two to three fibers, in the most peripheral zone of the SVN where small neurons popu late the nucleus (Fig 26) These fibers were also seen to give off fine collaterals extending medially across the SVN Many of these fine ascending fibers continued on into the cerebellum However the number doing so was less than that entering the nucleus so that some of these fibers probably terminated in the peripheral zone of the SVN

As the degenerated descending branches traveled in the dorsolateral part of the descending vestibular root they gave off fine collaterals medially in the regions of the caudal ventral LVN and the rostral DVN much as the heavy fibers did in previous animals They also appeared to end in similar areas of the DVN and MVN However the pattern of degeneration was more diffuse around the many smaller neurons in these nuclear groups

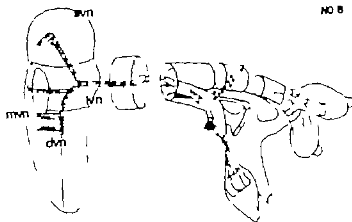


Fig. 27 Dra ing of the reconstructed lesion nd degenerati pattern in imal 8. The broken l nes represent both mall nd large size degenerating fibers.

B *Inf rior Division* (Posterior semicircular canal)

Because of the smaller size of the ganglion to the posterior canal and because there was n practical way of creating selective lesions of large or small fibers in this nerve even the smallest lesions in this ganglion involved both large and small fibers. The description of this lesion therefore co n-cerns both large and small fiber components to the posterior canal crista.

Cat 8 (Fig 27) In this animal the lesion was produced by application of the unipolar electrode tip onto the very caudal aspect of the vestibular ganglion as it arched over the cochlear nerve trunk. This part of the ganglion is solely concerned with posterior canal innervation and afforded an excellent opportunity of creating a selective posterior canal lesion A current of 2 milliamps was pplied for 3 seconds in this animal Postoperatively the animal exhibited a mild rotatory nystagmus which lasted 2 to 3 days. A survival period of 6 days was allowed before the animal was sacrificed by perfusion.

(*a*) *Le ion and peripheral degeneration* The lesion was found to involve the caudal end of the inferior vestibular ganglion (Fig 28 *A*) Degenerated fibers of various diameters were seen only in the posterior canal nerve (Fig 28 *B*) Degenerated axon could be followed proximally from the lesion coursing toward the rostral half of the vestibular trunk

(*b*) *Central degeneration* The degenerated axons were seen to occupy a narrow zone tretching the medio-lateral width of the vestibular root just rostral t the olivo-cochlear bundle (Fig. 29) These fibers gave off short collaterals, terminating in the caudal division of the interstitial nucleus of th vestibula root (Fig. 30) The incoming axons continued on over the

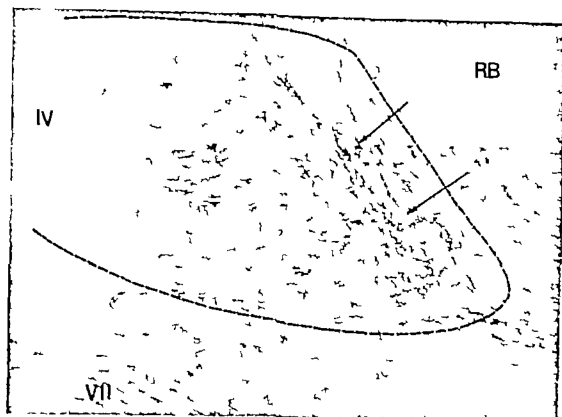


Fig 26. Trans rse section through th SVN f lmal 5 dem n trating the loc ti n of ascendi g bra hes of deg erati g mall fibers in the lateral a pect f the nu l us. Compare with Fig 16 and 21 Broken line d limit the SVN

ular root (Fig 25) terminated by means of collaterals on the rostral division of the interstitial nucleus, and finally bifurcated into ascending and descending branches at a more dorsal and lateral point than the larger fibers described in animals 56 and 49

The ascending branches of the small degenerating axons abruptly turned dorsalward and coursed as individual fibers, or packets of two to three fibers, in the most peripheral zone of the SVN where small neurons populate the nucleus (Fig 26) These fibers were also seen to give off fine collaterals extending medially across the SVN Many of these fine ascending fibers continued on into the cerebellum However the number doing so was less than that entering the nucleus so that some of these fibers probably terminated in the peripheral zone of the SVN

As the degenerated descending branches traveled in the dorsolateral part of the descending vestibular root they gave off fine collaterals medially in the regions of the caudal ventral LVN and the rostral DVN much as the heavy fibers did in previous animals They also appeared to end in similar areas of the DVN and MVN However the pattern of degeneration was more diffuse around the many smaller neurons in these nuclear groups.

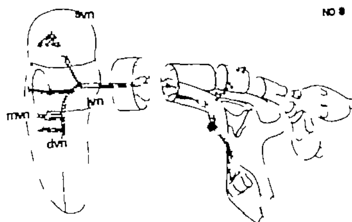


Fig. 27 Dra ing of the reconstructed lesi nd degeneration pattern in imal 8. The broken lines represent both small nd larg siz degenerati g fibers.

D. *Inferior Division* (Posterior semicircular canal)

Because of the smaller size of the ganglion to the posterior canal and because there was no practical way of creating selective lesions of large or small fibers in this nerve, even the smallest lesions in this ganglion involved both large and small fibers. The description of this lesion, therefore con cerns both large and small fiber components to the posterior canal crista.

Cat 8 (Fig 27) In this animal the lesion was produced by application of the unipolar electrode tip onto the very caudal aspect of the vestibular ganglion as it arched over the cochlear nerve trunk. This part of the ganglion is solely concerned with posterior canal innervation and afforded an excellent opportunity of creating a selective posterior canal lesion A current of 2 milliamps was applied for 5 seconds in this animal. Postoperatively the animal exhibited a mild rotatory nystagmus which lasted 2 to 3 days. A urvival period of 6 days was allowed before the animal was sacrificed by perfusion.

(*a*) *Lesion nd peripheral degeneration* The lesion was found to involve the caudal end of the inferior vestibular ganglion (Fig 28 *A*) Degenerated fibers of various diameters were seen only in the posterior canal nerve (Fig 28 *B*) Degenerated axon could be followed proximally from the lesion coursing toward the rostral half of the vestibular trunk.

(*b*) *Central degen ration* The degenerated axons were seen to occupy a narrow zone stretching the medio-lateral width of the vestibular root just rostral t the oli o-cochlear bundle (Fig. 29) These fibers gave off short collaterals, terminating in the caudal division of the interstitial nucleus of the vestibular root (Fig. 30) The incoming axons continued on over the

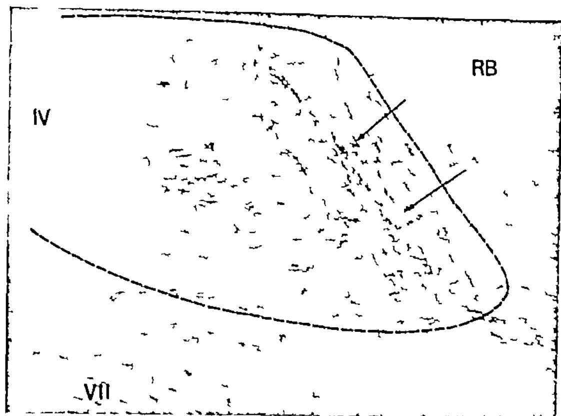


Fig 26 Tra erse secti through the SVN f anim l 5 dem n trating the loc ti n f scending branches of deg erati g mall fibers in th lateral pect f the nucleus. Compare with Fig 18 and 21 Broken lin d limit th SVN

ular root (Fig 25) terminated by means of collaterals on the rostral division of the interstitial nucleus, and finally bifurcated into ascending and descending branches at a more dorsal and lateral point than the larger fibers described in animals 56 and 40

The ascending branches of the small degenerating axons abruptly turned dorsalward and coursed as individual fibers, or packets of two to three fibers, in the most peripheral zone of the SVN where small neurons populate the nucleus (Fig 26) These fibers were also seen to give off fine collaterals extending medially across the SVN Many of these fine ascending fibers continued on into the cerebellum However the number doing so was less than that entering the nucleus so that some of these fibers probably terminated in the peripheral zone of the SVN

As the degenerated descending branches traveled in the dorsolateral part of the descending vestibular root, they gave off fine collaterals medially in the regions of the caudal ventral LVN and the rostral DVN much as the heavy fibers did in previous animals. They also appeared to end in similar areas of the DVN and MVN However the pattern of degeneration was more diffuse around the many smaller neurons in these nuclear groups

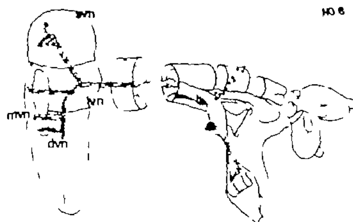


Fig. 27 Drawi g of the reconstructed lesion nd degeneration pattern in imal 8. The broken lines represent both mall and l rge size degenerating fibers

B. *Inf rior Division* (Posterior semicircular canal)

Because of the smaller size of the ganglion to the posterior canal and because there was no practical way of creating selective lesions of large or small fibers in this nerve, even the smallest lesions in this ganglion involved both large and small fibers. The description of this lesion, therefore concerns both large and small fiber components to the posterior canal crista.

Cat 8 (Fig 27) In this animal the lesion was produced by application of the unipolar electrode tip onto the very caudal aspect of the vestibular ganglion a it arched over the cochlear nerve trunk. This part of the ganglion is solely concerned with posterior canal innervation and afforded an xcellent opportunity of creating a selective posterior canal lesion A current of 2 milliamps was applied for 5 seconds in this animal I ostoperatively the animal exhibited a mild rotatory nystagmus which lasted 2 to 3 days. A urvival period of 6 days wa allowed before the animal was sacrificed by perfusion

(a) *Lesion and peripheral degen ration* The lesion was found to involve the caudal end of the inferior vestibular ganglion (Fig 28 *A*) Degenerated fibers of various diameters were seen only in the posterior canal nerve (Fig. 28 *B*) Degenerated axons could be followed proximally from the lesion coursing toward the rostral half of the vestibular trunk.

(b) *Central degeneration* The degenerated axons were seen to occupy a narrow zone tretching the medio-lateral width of the vestibular root just rostral to the olivo-cochlear bundle (Fig. 29) These fibers gave off short collat rals, terminating in the caudal divi ion of the interstitial nucleus f the vestibular root (Fig 30) The incoming axons continued on over the

SG

S

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A



Fig 28 1 ll rl t l secti f Scarpa ga gll n l l al 8 h wi g the lesi (*L*) l ll b n lle f d g erati g n (*arrow*) pa i g ce trally *B* High pow ph to-micrograph of tl ers t post rl l rl t howi g deg nerating fibers f ll l es

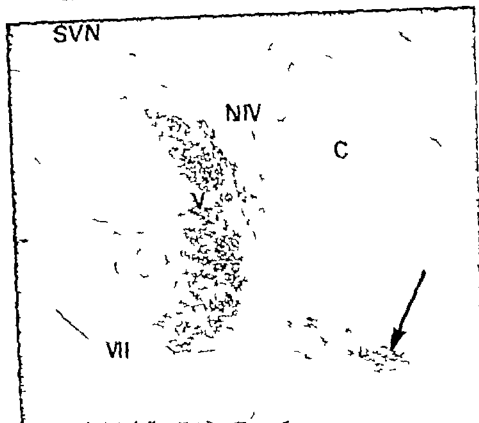
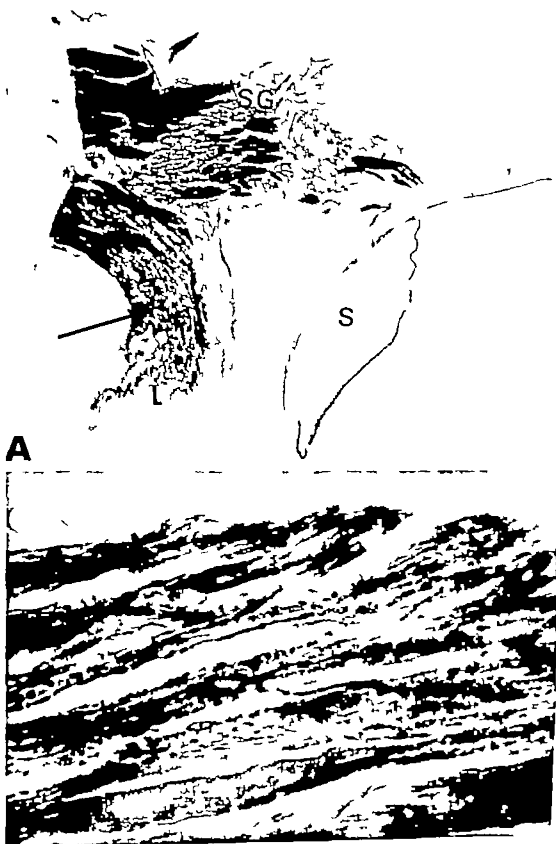


Fig. 29. Transverse section of the brainst m f imal 8 showing bundl of degener ting fibers (arrow) in the rostral part of the est bular root. The rostral di ision of the NIV ca be seen here and in Fig. 30 A.

dorsal aspect of the descending trigeminal root and actually extended into the lateral portion of the ventral LVN before undergoing the classical bi f rcation into ascending and descending rami this was the most medial bifurcation of any primary vestibular afferent fibers.

The ascending branches turned sharply upward and rostrally tra ersing the rostral part of the LVN to enter the caudal part of the SVN. In this nucleu these degenerated axons constituted the most medially located fibers passing through the central zone. A they reached the midporti n and dorsal half of the nucleus hort collaterals were given off which extended medially and ventrally down onto the laminar arrangement of cells in the medial part of th nucleu (Fig. 31). The ascending rami then terminated round large cell in the medial part f the central zone of the SVN. It could not be determined with certainty whether some of these degenerating fibers continued on int the cerebellum.

At the very point that the degenerating descending branches could be recognized caudal to the bifurcation of incoming axons, long collaterals



F g 28 A Il ri tal secti f Sc rpa ga gli in im 1 8 h wi g the l (I) nd the b dl f leg erati g x (ro) pa l g ce trall B Higl pow ph to- micrograpl f tl rs t po teri ca l eri t l wi g deg n rati g fibers f ll lres

A ta to-l gng S ppl 51

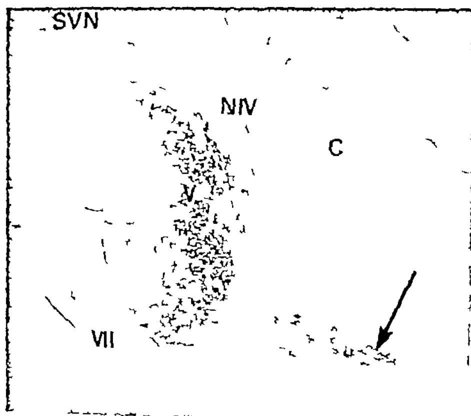


Fig. 29. Transverse section of the brainstem of animal 8 showing bundle of degenerating fibers (*arrow*) in the *rostral* part of the vestibular root. The rostral division of the VIII can be seen here and in *Fig. 30 A.*

dorsal aspect of the descending trigeminal root and actually extended into the lateral portion of the ventral LVN before undergoing the classical bifurcation into ascending and *descending rami*; this was the most medial bifurcation of any primary vestibular *afferent fibers.*

The ascending branches turned sharply upward and *rostrally*, *traversing* the rostral part of the LVN to enter the caudal part of the SVN. *In this nucleus these* degenerated axons constituted the most medially located fibers passing through the central zone. As they reached the midportion and dorsal half of the nucleus *short collaterals* were given off which extended medially and ventrally down onto the laminar arrangement of cells in the medial part of the nucleus (Fig. 31). The *ascending rami* then terminated around large cells in the medial part of the central zone of the SVN. It could not be determined with certainty whether some of these degenerating fibers continued on into the cerebellum.

At the very point that the degenerating descending branches could be recognized caudal to the *bifurcation of* incoming axons, long collaterals

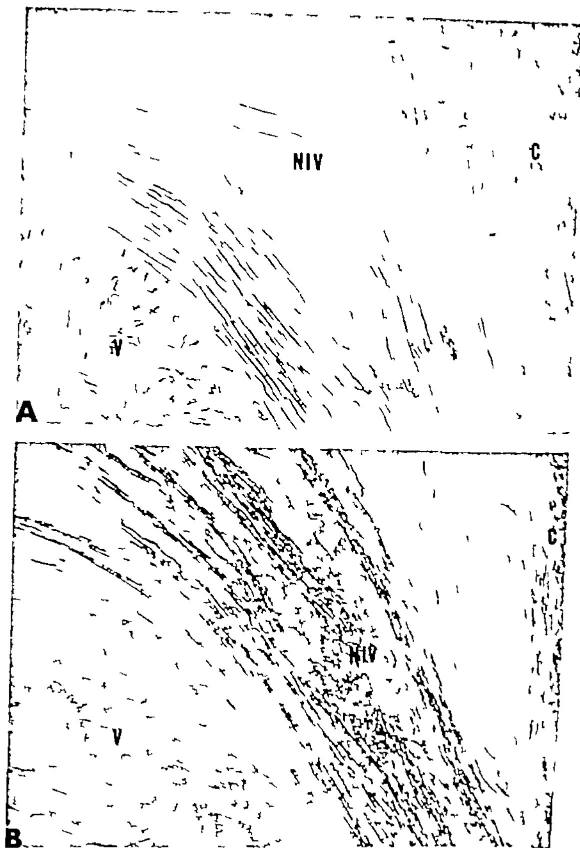


Fig 30 4 Rostral di i l n f th NIV in l 1 8 h wl g bsence f deg eratl B, Ca d l di l l f the NIV in same lmal d m strati g collat ral terminal degen ra tio from degen ratl g ax in th estibula root Compare with Fig 17

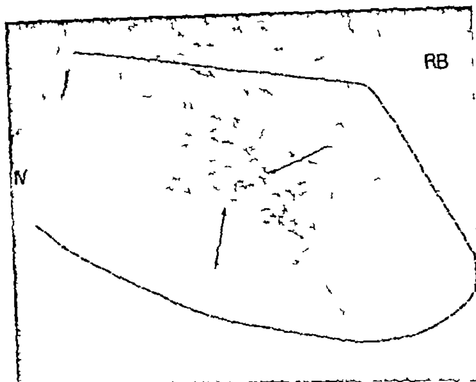


Fig. 31. Transverse section through the SVN (d limited by brok line) 1 ... 2. The degenerating ascending branches ... the medi l-central part of the nucleu ... ad th ir collaterals (arrows) can be seen. Not the absence of degeneration ... the central–lateral and ... entral regions of the ... uclea where superior and horizontal canal fibers terminate.

were seen travelling obliquely ... cross the ventral LVN to terminate on small ... er cells at the medial margin of the LVN and on cells in the dorsal part of the adjacent MVN (Fig. 32).

The degenerating descending rami were well localized at the most medial and dorsal aspect of the descending vestibular *root* (*Fig. 33*). As these fibers coursed more caudally collaterals were given off at the level of the rostral DVN. These collateral ... traveled medially across the DVN at a slightly more dorsal level than those from the superior division lesions ... although a few preterminal patt rns were seen around small and medium cells in this nuclei ... the large cell ... were ... trikingly free of terminals from these collaterals. The collaterals then continued on through the DAS to terminate on cell ... in the ventral part of the MVN at this level. As more caudal levels of th ... DVN were reached, the descending branches assumed a more diffuse arrangement in the medial part of the descending vestibular root and gave off scattered collaterals to the DVN and MVN. Again at very caudal levels ... f these nuclei, descending cerebellar degeneration precluded *demonstration* ... f precise termination of ... estibular afferents.

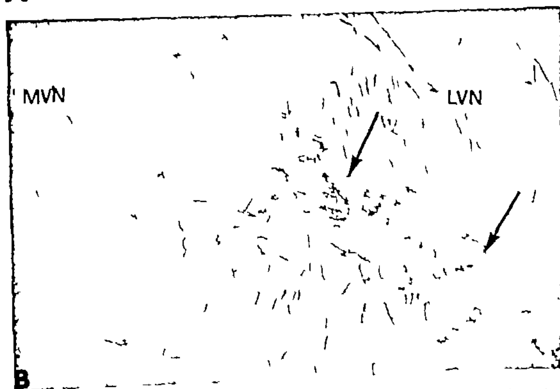


Fig 32 A Tran erse section through the LVN of anim l 8 at the l vel f l coming deg ne atl g fibers Coll teral rl l g e th bif rcatl point (*arrow*) pa thro gh th LVN to the MVN nd adj ce t LVN *B* High power ph t micrograph f th squared area in (*A*) l wi g th t rn l tl n f coll teral (*a rows*) l MVN nd dj ce t LVN

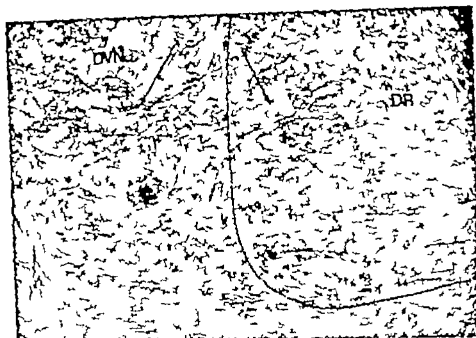


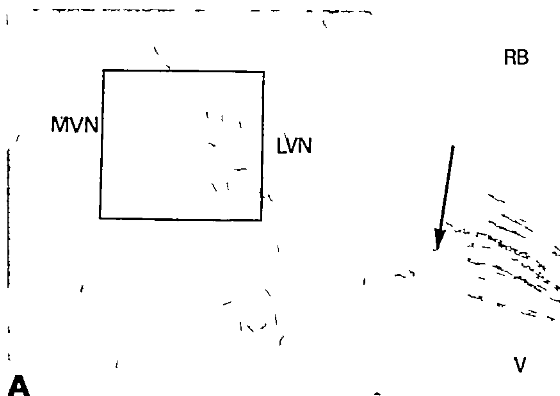
Fig. 33. A tra nsverse section through the descendi g vest bular root (———————) nd nucleus f animal 8. Le 1) comparable t that f Fig 22. Note the degenerating descendi g branches i the medial aspect of descending vestibul root nd their collateral (arrows) directed medially. The clea entral rea l the root and nucleus re occupied by normal superior nd horizontal can l fibers.

OTOLITH ORGANS

A. Utricle

Cat 33 (Fig. 34) The lesion in this cat was made by directing a small straight needle vertically down through the caudal part of the superi r division ganglion. In this way the cell mass providing small fibers to the superior and horizontal canals s well as the ventral cell mass innervating the utric ular macula were involved. Postoperatively no gross nystagmus was noted, whil som ataxia was evident. The animal wa perfused 6 days after surgery.

(*a*) *Le ion and peripheral degeneration.* A discrete lesion was found which extended the entire d rsoventral dimension of the caudal one-third f the uperior division ganglion (Fig 35 A and 36). Only very small-caliber fibers howing advanced wallerian degeneration were seen peripherally in the uperior di isi n. In dorsal section through the superior division the degenerated fibers were arranged as a compact group which were then seen t di erge a the tw mpullary nerves were formed. These diverging fibers encircled th normal larger fibers coming from the rostral part of the uperior ganglion nd were then seen a degenerated fine fibers located in



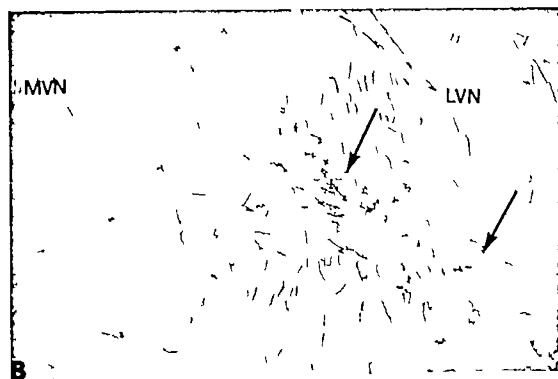


Fig 32. (Tran rs sect thro gh th LVN f a imal 8 t th l el f l ml g deg n rating fibers. Coll teral rl l g n the bifurcatl n poi t (row) pass thro gh the LVN to the MVN a d adj ce t LVN B High-power phot micrograph f the sq red rea in (A) h wing th t i ti f coll t ral (arrows) i MVN nd dj ce t LVN

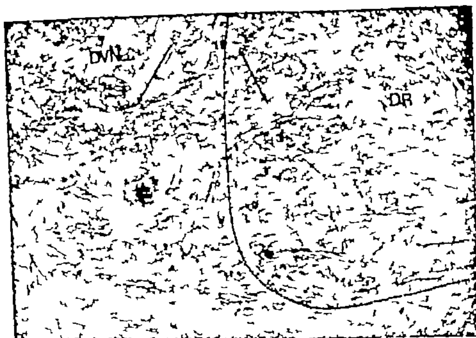


Fig. 23. A transverse section through the descending vestibular root (————) and nucleus of animal 8. Level is comparable to that of Fig. 22. Note the degenerating descending branches in the medial aspect of descending vestibular root and their collateral (arrows) directed medially. The lateral area of the root and nucleus are occupied by normal superior and horizontal canal fibers.

OTOLITH ORGANS

A. *Utricle*

Cat 35 (Fig. 24). The lesion in this cat was made by directing a small straight needle vertically down through the caudal part of the superior division ganglion. In this way the cell mass providing small fibers to the superior and horizontal canals as well as the ventral cell mass innervating the utricular macula were involved. Postoperatively no gross nystagmus was noted, while some ataxia was evident. The animal was perfused 6 days after surgery.

(a) *Lesion and peripheral degeneration.* A discrete lesion was found which extended the entire dorsoventral dimension of the caudal one-third of the superior division ganglion (Fig. 35, 1 and 30). Only very small-caliber fibers showing advanced wallerian degeneration were seen peripherally in the superior division. In dorsal section through the superior division the degenerated fibers were arranged as a compact group which were then seen to diverge as the two ampullary nerves were formed. These diverging fibers encircled the normal larger fibers coming from the rostral part of the superior ganglion and were then seen as degenerated fine fibers located in

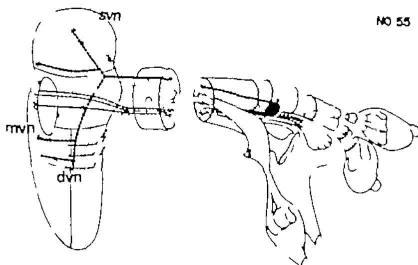


Fig 34 Drawi g of the reconstructed l si n and deg n ration pattern in animal 55 The ingle heavy brok line rep esent the deg n rati g proximal ax n used by a second ary lesion.

the periphery of each ampullary nerve (Fig 35 B) *Degenerated fibers cours ing proximally from this part of the lesion occupied the dorsal and caudal part of the rostral half of the vestibular nerve*

Careful reconstruction of the lesion also revealed a minute secondary *lesion involving only the central axons of the rostral ganglion cells of the* superior division (Fig 36 A) There was no degeneration of these cells or of the large fibers in the ampullary nerves. However a few degenerated large fibers coursed centrally in the rostral part of the vestibular nerve (See Fig 34)

As ventral levels of the superior ganglion were examined many degener ated small fibers were followed out in the utricular nerve toward the macula At these levels no degenerating fibers were seen in the remainder of the superior division The degenerated axons coursing proximally from the utric ular ganglion were compactly arranged and directed caudo-medially to locate in the ventral part of the caudal division of the vestibular nerve trunk (Fig 36 B)

In the vestibular nerve trunk then two separate bundles of degenerated axons were seen coming from the single lesion in Scarpa s ganglion the one bundle in the dorsal part of the rostral division was related to the small *fiber ganglion population of the canal nerves* as was seen in cat 5 the other bundle occupying the rostroventral part of the caudal division represented the degeneration from the injury to the utricular ganglion cells.

(*b*) *Central degeneration* Brainstem sections clearly revealed two bundles of degenerating *axons in the vestibular root* (Fig 37) As the root entered the brainstem the dorsal and rostral group (small canal fibers) occupied the lateral aspect of the root while the ventral-caudal group of fibers became

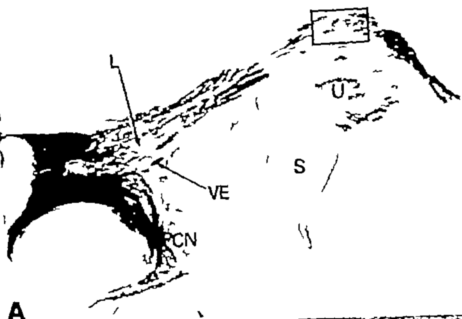
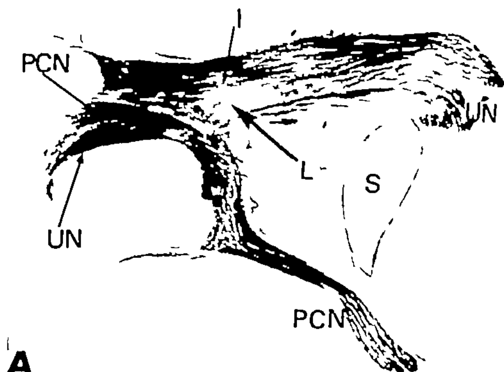




Fig. 33. *A*, Horizontal section through the dorsal aspect of the lesion (*L*) in animal 45. Note the efferent vestibular fibers (VE) spared by the lesion. Ampullary nerve in the square is shown in Fig. 33 *B*. *B*, High-power magnification of superior canal nerve showing the degenerating small myelinated fibers at the periphery (*arrows*) while the larger fibers in the center are intact. Compare with Fig. 13.

the most medially placed fibers in the caudal part of the root. A few degenerated large axons occupied the rostral part of the root.

The degeneration pattern of the dorsal-rostral group of small caliber fibers and the few large fibers in the rostral part of the nerve followed those in



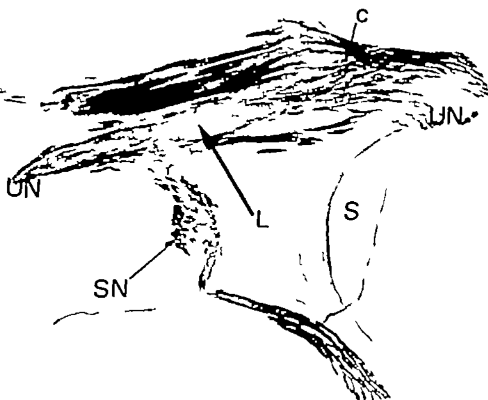


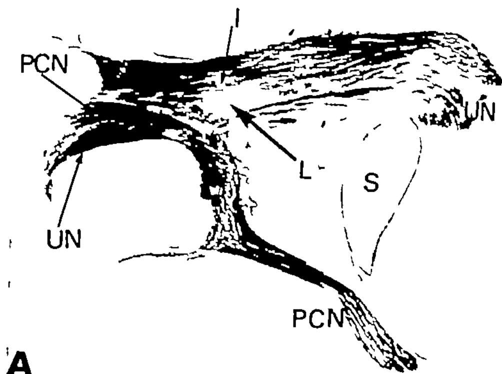
Fig 36 t Il I t I secti thro gh th ce ter f lesi (I) I nimal 53 Not sec da I (I) i terrupt g I th ce tral a f ro tral g gli n lls. B, Il ri t t ecti n thro gl the tral part f th lesi n (I) f nim l 53 Thi I the pa t f Sc pa ga gli n whi h pplies th utri l Note the degen rati n xt ndi g pe ipherall d trall t the lesi N t lso th co ergence f list l proce es of ea I g gli cell ( ) wi Il the central processes t k traightf rw rd co rse t w rd the brain t m

Fig. 37 Transverse section through the brain stem and vestibular root of animal 55. There are two separate bundles (arrows) of degenerating axons in the vestibular root.

animals 6 and 56 respectively. A complete description of these groups will therefore not be repeated since their importance here is only to permit distinction between these canal fibers and those from the utricular macula. This animal did demonstrate however the separate localization of the two fiber groups in the SVN and also the importance of careful reconstruction of the lesion and the degenerating fibers peripheral as well as central to this lesion.

The central and caudal group of fibers represented central degeneration from the utricular ganglion lesion. These fibers remained as a compact bundle hugging the lateral aspect of the trigeminal root (Fig. 38 A). In this caudal part of the vestibular root, no recognizable part of the interstitial nucleus was seen. However an occasional solitary large neuron was present. Although the utricular fibers passed immediately adjacent to these neurons no evidence of termination was seen (Fig. 38 B).

These degenerating utricular axons bifurcated more laterally than any other vestibular neurons. From reconstruction of serial sections it was seen that the ascending rami curved gradually in a rostral direction to the rostro-



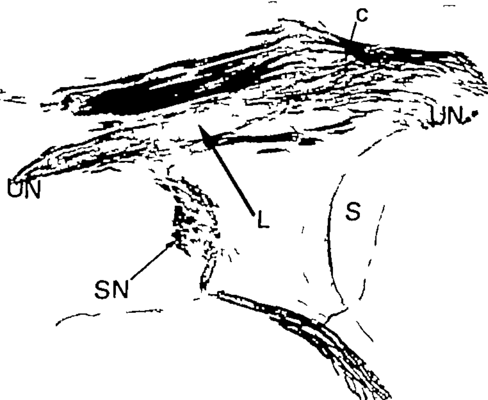


Fig 36 4 II ri nt l secti thro gh th center f l l (L) l lm l 55 N t h secondary l t (I) l terrupting nly the ce tral f rostral g ngli cell B II ri t l secti n through the v tral part f th lesl (I) f lm l 55 Thi l the part f Sc rpa g gli wl l h upplies the utri l Not the d g rati n t ndi g periph ll nd centrally t th lesl Not lso th co erg nce f distal processes f canal g gli ll ( ) whil th tral processes t k traightf rward rse t ward th brai t m.

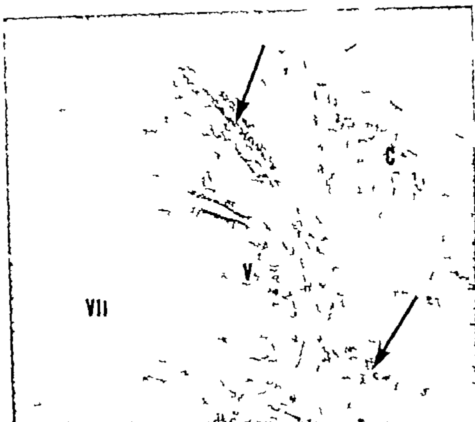


Fig. 37 Tra sverse section through the brainst m and vestibular root of nimal 35 There are tw separat bu dles (arrows) of dege erating xons i the estibular root.

animals 5 and 6 respecti ely A complete description of these groups will therefore not be repeated since their importance here is only to permit distinction between these canal fibers and those from the utricular macula. Thi animal did dem n trate howev r the separate localization of the two fiber gr ups in the SVN nd also the importance of careful reconstruction of the lesion and the degenerating fibers peripheral as well as central to this lesion

The ventral and caudal group of fibers represented central degeneration from the utricular gangli n l si n These fibers remained as a compact bundle hugging the lateral a pect f the trigeminal root (Fig 38 *A*) In this caudal part f the estibula root, no recognizable part of the interstitial ucleu wa seen. Howe er an occasional solitary large neuron was present Alth ugh the utricular fibers pa sed immediately adjacent to these neurons no evidence of termi ation wa seen (Fig. 38 *B*)

These degenerating utricular ax ns bifurcated more laterally than any other l bular neur n From reconstru tion of serial sections it was seen that the ascending mi curved graduall in a rostral direction to the rostro-

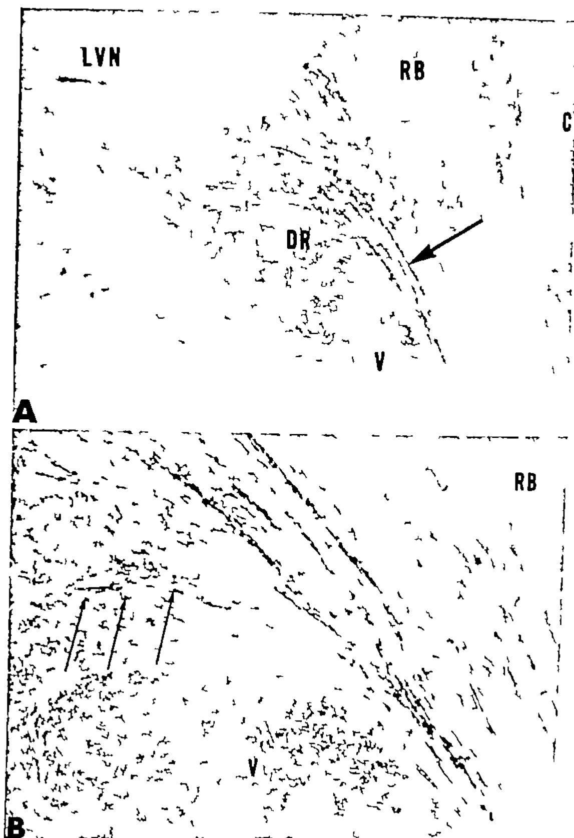


Fig 38 *A* Tra erse secti thro gh th brai t m f a im l howi g th deg rati g utricul fibers (*a row*) th te the stib la u l l *B* High-pow ph t micrograph f th utri ula fibers l (4) d m trati g how the cell in tl es- tibul root d n t recei t rmi l fro these fibers. N t also how tl desc ndi g br n hes f th tri ul fibers ( ) occ py most l t ral positi n i th d sce d ing vestib l ro t

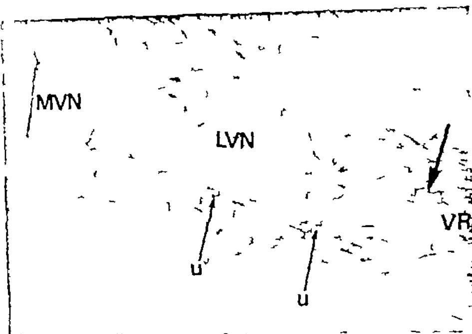


Fig. 39. Trans erse section of the LVN d the MVN f nimal 55. The course nd termination of the scending branches f degenerating tricula fibers ( ) in these nclei can be seen. The descending branches of th degenerati g rostral canal fibers re seen as black dot 1 the dorsal aspect of the vestibular root (arrow)

ventral part of the LVN and tra eled directly across this nucleus toward the MVN (Fig 39) A few of the medium sized neurons in the ventral LVN showed preterminal and terminal degeneration from these degenerated ascending branches (Figs. 40 A 41) The major terminal of these ascending branches, however appeared to be in the rostral part of the MVN where preterminal degeneration was seen on large and small neurons in the lateral half of the nucleus (Fig. 40 B)

The descending branches were seen as degenerating fibers coursing in the most lateral and ventral part of the descending vestibular root (Fig. 38 B) Collaterals were gi en off by these descending fibers and filtered through the descending root fibers to enter the rostral DVN where they ppeared to contact the same cellular areas as the semicircular fibers. The numerou scattered neurons in th descending vestibular root did not receive ny termination from these utricul r fibers.

The question of whether these collaterals from the descending utricular branches ent r the adjacent MVN was difficult to determine because of the degeneration there from the canal fibers involved in this animal. The mount of terminal degeneration in thi part of MVN however did not ppear t be significantly increased over that seen in cat 5 However the possibility remain that some utricular axons terminated in this area. Again

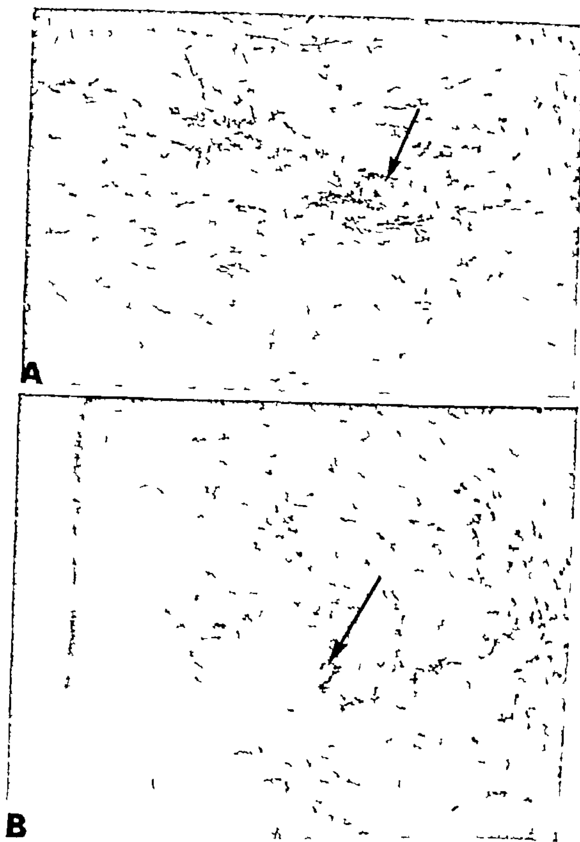


Fig 40 A High power phot micrograph f th LVN in the previ u figure dem nstrati g ntricul x n with som preterml l degenerati n ron d medi m ized cell (rrow) *B* High power phot micrograph f th MVN i Fig 39 howing t rmi ati n f degen rat ing nt icul r fibers n both mall nd medium ized euron (*arrow*)

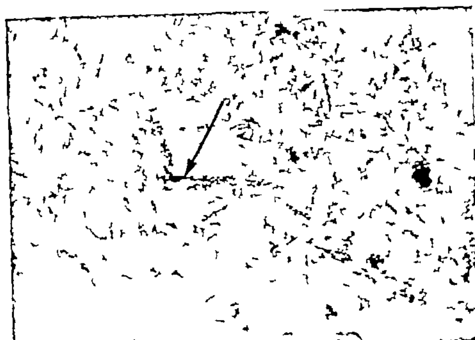


Fig 41 High-power phot micrograph thro gh the caudal part of the ventral LVN i animal 53. Arrow point t large neuron with terminal nd preterminal degeneration from the utricular lesion. These degenerati g fibers by pass most of the cell i the nclea t the right of the field.

the more caudal half of the DVN and MVN was difficult to evaluate because of diffuse descending cerebella degeneration.

B *Saccule*

Cat 30 (Fig 42) Since the saccular ganglion lies most ventral of all vestibular ganglion cells, it was impossible to involve it selectively without in

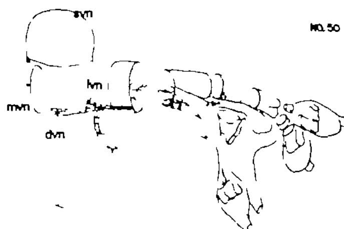
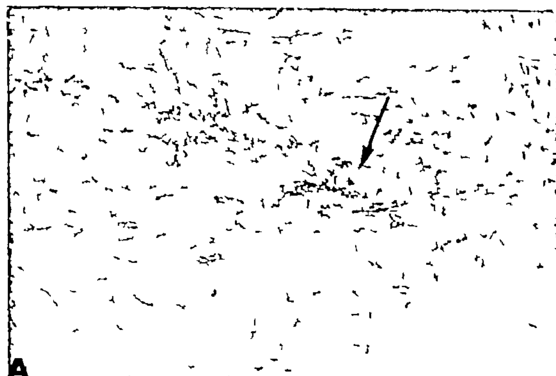


Fig 42. Dra g of the lesion nd degeneration pattern in animal 30.



B

Fig 40 A High powe ph t l rog ph f th LVN in the pre l a figure d n o trati g utricular with som pret m l deg rati n around medium l ed cell (a row) B High power ph t mi rograph f th MVN Fig 39 showing t rmination f deg n rat i g utricula fibe n both m ll a d medium-sized ne ro (arrow)



Fig. 41 High-power photomicrograph through the caudal part f the entral LVN i animal 55. Arrow point t large neuro with termi al nd preterminal degeneratio from the utricular lesion. These degenerati g fibers by-pass most f the cells i the nucle t the right of the field.

the more caudal half of the DVN and MVN was difficult to evaluate because of diffuse descending cerebellar degeneration.

B. *Saccule*

Cat 50 (Fig 42) Since the saccular gangli n lies most ventral of all vestibular ganglion cells, it was impossible to involve it selectively without in-

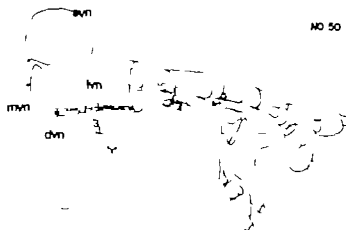
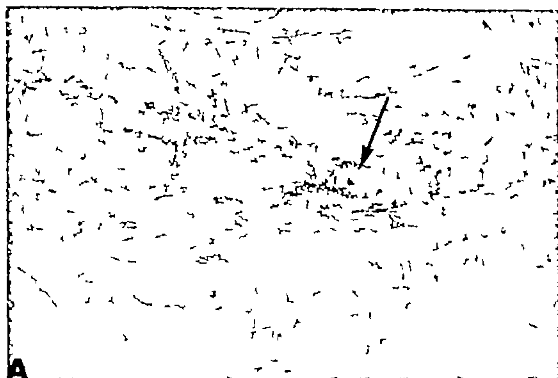


Fig 42. Dra i g f the lesion nd degeneration pattern i animal 50.



B

Fig 40 4 High pow ph t mi rograph f th LVN in th pre l us figure d m nat tl g utricul with som pret rminal d g eratl n aro d medi m l ed cell (rrow) *B* High pow ph t mi rograph f th MVN i Fig 30 howi g t rmi tl f d g n rat i g utricul fibers o both mall nd medium-sized uro (*arrow*)



Fig. 44. A, High-power photomicrograph of the ascending degenerating saccular fibers in animal 30 ... they travel through the LVN toward group "y". Note how the fibers ... by pass the cells of the LVN. B, High-power photomicrograph of group "y" in Fig. 43 with abundant degeneration in the nucleus. Compare with Fig. 11

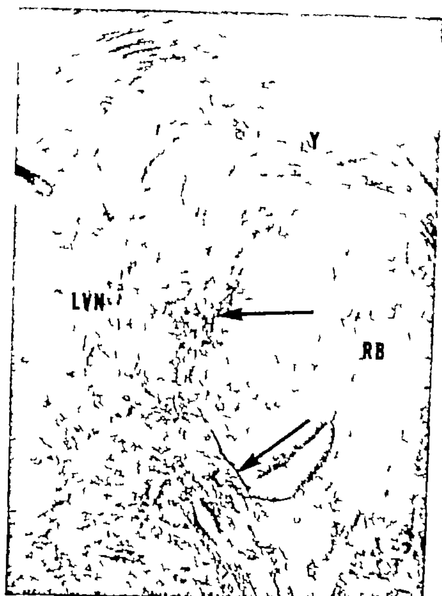


Fig 43. Transverse secti n through the ca dal nd of the estibul r root nd brainst m f nim l 50 The deg erating saccular fibers (*arrows*) can be seen coursi g dorsally just medial to the restiform body t ward group "y" nu l us.

juring the posterior canal fibers. However since it was clear from dissected normal specimens that the axons of the saccular nerve form the most caudal fibers of the vestibular nerve trunk it was possible to separate these caudal bundles and transect them with a small knife In this way a selective lesion of the saccular axons was created in cat 50 The animal displayed no nystagmus or marked vestibular upset except for that which was associated with cerebellar retraction The animal was allowed to survive only 4 days before perfusion fixation was performed

The short survival period of 4 days was allowed because it was found in other cats with saccular lesions that the small saccular fibers displayed

the ganglion and nerve trunk provided a basis upon which to direct the placement of lesions and to reconstruct the degeneration from these lesions.

In the peripheral vestibular branches Sudan Black reliably demonstrated myelin sheaths of extremely fine fibers of one micra or less in diameter. The axis cylinders of these fibers would be difficult to d monstrate consistently with silver techniques that must be applied after lengthy decalcification of the dense petrous bone of the cat. The Sudan Black technique as used in this study can be used to accurately measure these myelin sheath diameters because there is negligible shrinkage when frozen sections are made of these nerves (Gacek & Rasmussen, 1961).

The Nauta silver technique as modified by Rasmussen was used to demon strate the degenerating fibers in the vestibular root and brainstem. As the method is intended to selectively impregnate degenerated fibers, there is always the possibility of nonimpregnation of some abnormal fibers particularly small ones. The excellent report of Eager & Barnett (1966) provided a guideline to reduce this possibility to a minimum.

Evaluation of lesions in Scarpa's ganglion

Three principles were extremely important in the accurate evaluation of lesions in Scarpa's ganglion.

1. The urvival time following lesions must assure optimal demonstration of wallerian degenerati n in small as well as large fibers in the peripheral vestibular nerve. This period was five to seven days in the cat.
2. The exact extent of the lesion in the ganglion must be carefully recon structed from serial sections.
3. A comparison must be made between the number of degenerated fibers peripheral and c ntral to the lesion in Scarpa's ganglion.

The importan e of these principles i demonstrated by the following.

If a discr t lesion were made in the caudal part of the superior division ganglion deep enough to in olve the utricular ganglion cells as well as the d rsal group upplying m ll fibers to the horizontal and uperior canals and a survival time of 12 to 14 days allowed, the resulting degeneration would be e tremely difficult to evaluate. After this degeneration period, the extremely fine periph ral processes of the canal ganglion cells would have compl t ly deg nerated and p oduct of wallerian degeneration would not be demon trable while the larger central processes of the same cells and their continuation into the brain tem would be demonstrated. Superficial ev luation f th lesion would lead one to believe that the utricular ganglion pr ject centrally not only t the LVN DVN and MVN but also to the lateral port on f the uperi r vestibular nucleus—the area to wh ich the small fibers of the uperior and horizontal canal project.

However careful reconstruction of the lesion, and a comparison of the

such advanced degeneration at 6 to 7 days that it was difficult to follow the axonal debris central to their bifurcation in the brainstem

(*a*) *Lesion and peripheral degeneration* Since transection of the proximal process (axon) of the saccular ganglion cells was performed in the vestibular nerve trunk no peripheral degeneration was found in the saccular nerve or any other vestibular branches

(*b*) *Central degeneration* The central course of degenerating fibers from this saccular nerve lesion was unique The degenerating fibers formed the most caudal and dorsal component of the vestibular root As they proceeded in toward the vestibular nuclei they occupied the most lateral position in this caudal end of the vestibular root (Fig 43) Some fibers were so far lateral that they cut through part of the restiform body in an almost dorsal direction Most of the fibers, however continued along the medial surface of the restiform body until the caudal LVN was reached Here they bifurcated into very fine rami

The ascending branches continued on in a direct dorsal direction through the part of the LVN adjacent to the restiform body (Fig 43 and 44 A) These did not terminate on LVN cells, but by passed them and ended in the small groups of cells called group "y" by Brodal (Fig 44 *B*) This group of *cells overlay the dorsum of the restiform body and the dorsal LVN* Abundant degeneration was seen in this nucleus The degenerated saccular axons which coursed through the restiform body appeared to end directly in group "y" without bifurcating

Very fine descending branches from the incoming saccular fibers were seen to turn ventrally and medially from the point of bifurcation These fibers appeared to end on a few cells in the most lateral portion of the adjacent LVN and also on the most rostral end of the DVN At this point it was very difficult to tell where the LVN ended and the DVN began This degeneration in the LVN and the DVN from the saccular lesion was very modest Only the projection to group y was most impressive in the central *degeneration from this saccular nerve lesion*

DISCUSSION

Technique

The success of this study was felt to be largely dependent on a thorough knowledge of the anatomy of the *peripheral vestibular nerve and its branches* to the vestibular endorgans This included not only the relationship of the nerve rami to different parts of Scarpa s ganglion but also data on the diameters of the nerve fibers making up the vestibular complex The Sudan Black B method of Rasmussen proved *to be a suitable technique*

Familiarity with the vestibular nerve branches was obtained by dissecting a large number of normal ears. Dissection of the branches proximally into

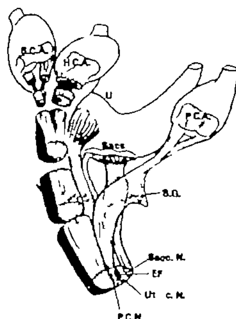


Fig. 41. Drawi g from dorsal ew of the right vestibula nerve ad endorga summarizing the peripheral location f first order neurons. The dark ad light rea in the superior division represent the location of large and small caliber neurons respectl el t the superior ad horizontal canal crist xpl ined text thi nerv is segmented I the drawing in order t demonstrat the cha ge i position of the large nd small fibers in the nerv trunks.

Projection f ve tibular endorgans

It was clear that the axons of ganglion cells innervating all three semicir cula canal cristae conv rged in the rostral division of the vestibular nerve trunk, while those from the two maculae formed the caudal division (Fig. 40) The compact bundles f fferent fibers to both cochlear and vestibular end rgan were interposed between these two divisions at the ventral aspect of the nerve

Cri ta Whil the neurons supplying the posterior canal crista were followed a a di tinct bundle from endorgan t central termination, it was clearly seen that the two canal of the uperior division did n t each have an ex lu iv part of Scarpa ganglion, nor did they each have a separate central termination. In tead, each of these cri t e was supplied by nerve fibers from tw part of the ganglion upplying the superior vestibular—a rostral one gi ing rise to large diameter nerve fibers and a caudal-dorsal on gi ing rise t small nerve fibers. Even a very mall lesion in each of these pa t f the ganglion produced approximately equal amount f degen ration in the n rves t each f these two canal cristae In terms of inner tion the canal portion f the superior divi ion can be considered as one canal nerv with two separate sensory areas. Phylogenetically this repre

number of degenerating fibers proceeding peripherally from the lesion with the number coursing centrally into the brainstem would alert the observer to the fact that an accurate correlation between endorgan and brainstem cannot be made. Of course a much shorter degeneration period would have obviated much of the difficulty in such a case

Vestibular efferent fibers involved in lesions of Scarpa s ganglion

The possibility of vestibular efferent fibers interrupted by lesions in Scarpa s ganglion was considered Lesions involving the caudal part of the *superior division ganglion* and those involving the ganglion to the posterior canal were the only instances in which this factor need be taken into account Thorough knowledge of the number course and distribution of vestibular efferent fibers, at all levels of the vestibular nerve complex (Gacek 1960 1966 1967) was most helpful in accurately evaluating such lesions Discrete lesions were made in the caudal part of the superior division ganglion without involving the main bundles of vestibular efferent fibers (see Fig 35 4) The small degenerating fibers emanating from such a lesion were at least almost entirely afferent dendrites Furthermore all efferent fibers would account for only a small fraction of the small sized fibers in the ampullary nerve branches

Cerebellar degeneration in the evaluation of brainstem projections of vestibular endorgans

As shown in the control group of cats, significant cerebellar cortical degeneration was produced from retraction of the flocculus and adjacent cerebellum However for the most part this did not present a problem in the vestibular nuclei The areas such as the ventral part of the LVN all except the most rostral and dorsal part of the SVN all except the caudal half of the MVN and the DVN and the smaller nuclear groups (such as the MV and group 'y) were free of such descending cerebellar degeneration even in the severest of the control group

In the most rostral and dorsal part of the SVN and in the caudal half of the MVN and DVN diffuse terminal cerebellar degeneration was consistently present and precise statements about the primary vestibular projections to these areas could not be made Therefore the caudal regions of the MVN and DVN were left *blank in the summary diagrams (Figs. 40, 47)* and a question mark was placed over the possible continuation of large semicircular canal fibers from the rostral SVN into the cerebellum It can be stated, however that the descending rami and collaterals of all endorgans except the saccule, did project caudally beyond the part of the MVN and the DVN shown in the diagram but that in these areas the termination on cells in the lateral part of the MVN and the medial DVN was very diffuse and became indistinguishable from that of the degenerating cerebellar cortical axons.

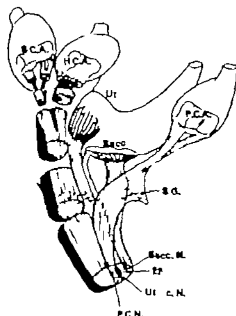


Fig. 45. Dra ing from dorsal view of the right estibula nerve and endorgans sum mari ing the peripheral location f first ord neurons. The dark nd light rea t the superior di ision represent the location f larg nd small caliber neurons respectivel t the superior nd horizontal canal crista explained i text this nerv i segmented i the dra i g i order t demo strat the cha ge i positio of the l rge nd small fibers the nerve trunks.

Proj ction of vestibular endorgans

It was clear that the a ns of ganglion cells innervating all three semicir cular canal cristae converged in the rostral division of the vestibular nerve trunk, while those from the two maculae formed the caudal division (Fig 45). The compa t bundles of efferent fibers t both cochlear and vestibular endorgans were interposed between these two divisions at the ventral aspect f the nerve

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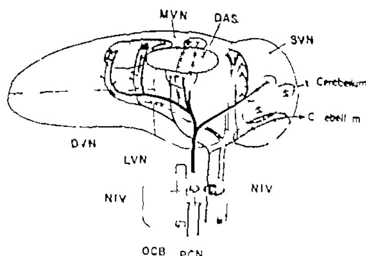


Fig 46 Line drawing summarizing the central course and terminati n f semicircular canal neurons in th vestibular nucl i (See t xt for xpl nati n of differe t ized lines)

sented the anterior (superior) of the two vertical canals present in lower vertebrates which in higher vertebrates formed the newer horizontal canal by merely splitting off another sensory area

Because of the separate ganglionic masses supplying large and small fibers to this canal it was possible to describe its central projection in terms of large and small fibers Of course the po terior canal neurons also have large and small fiber components, but it was not possible to selectively destroy each of these because of the smaller size of the ganglion to this endorgan Therefore the posterior canal central projection described con cerned both large and small fibers The diagram (Fig 46) represents these canal fibers by relative differences in the fibers, e g the large and small fibers of the superior division canals are represented by very wide and very thin lines, while the posterior canal projection is represented by a line of intermediate size

As the canal fibres entered the brainstem in the vestibular root those of the superior division canal were associated with and terminated by means of short collaterals on the cells in the rostral division of the NIV while those of the posterior canal had a similar correlation to the caudal division of the NIV Only semicircular canal fibers were associated with this classical nucleus and no macular (utri le or saccule) fibers terminated here A smaller more peripherally located nucleus, in the vestibular root described by Fuse (1912) also received semicircular canal fibers collaterals this nucleus was made of very small cells in contrast to those in the classical NIV The projection of the NIV is not completely clear although there is some evidence that it like the LVN projects down to the spinal cord (Bro dal & Pompeiano 1957) Clearly though it is a nucleus concerned solely with semicircular canal innervation

The course and termination of the ascending rami of the posterior canal

and the superior division canal were distinctly different. The posterior canal fibers bifurcated most medially of all the vestibular fibers. As a matter of fact, this bifurcation occurred within the lateral part of the LVN. The ascending branches proceeded through the LVN and entered the central and medial part of the caudal SVN. These fibers then ascended to approximately midway between the dorsal and ventral limits of the SVN and terminated primarily on medium to large cells in the central-medial region and, by way of short collaterals that extended ventromedially onto a lamina of cells reaching the medial limits of the nucleus. The superior division fibers bifurcated more laterally and rostral to the posterior canal fibers, and, accordingly, the ascending branches entered and terminated in the central lateral and rostral parts of the SVN. However, these branches gave off long collaterals quickly upon entering the SVN and these collaterals arched medially and dorsally to terminate on the same horizontal lamina of cells in the medial part of the nucleus which received collateral innervation from the posterior canal fibers. In the SVN, then, there appeared to be cell groups which received separately the fibers of the posterior canal and superior division canal and also cells which received collateral innervation from both these canals.

Descending branches from the two canals also were localized separately in the descending vestibular root. Similar collaterals to the other nuclei were formed from the fibers of both canals, but, as a rule, the collateral fibers and innervation of the superior division canal were located just ventral to those of the posterior canal. This held true except for the mid- and caudal regions of the MVN and the DVN, where the fibers of all the canals were diffusely mixed.

The termination of the large and small afferent fibers of the superior division canal, particularly in the SVN, was most interesting. The large fibers traveled up the central part of the SVN and terminated on the larger cells there while the small fibers occupied the small-celled peripheral zone between the center and the restiform body and probably ended on some of these small cells. While it was not possible to determine whether the large fibers proceeded also to a cerebellar termination, it was certain that some of the fine fibers did continue on into the cerebellum.

Since morphologically the large fibers appear likely to form the large calyx-like endings on type I hair cells in the cristae while the small ones, along with the small efferent fibers, make contact with the phylogenetically older type II hair cells (Wersäll, 1960), there is an indication that the different hair cell types have distinctly *different* central terminations and, therefore, different functional considerations.

Additional support for such a functional *difference* between the two types of vestibular hair cells has come from the numerous reports on the ototoxic effect of streptomycin sulfate. It is well known that the streptomycin effect both in human subjects (Schuknecht, 1958; Graybiel *et al*., 1962) and in the laboratory animal (Schuknecht, 1958) is measured by the elimination of

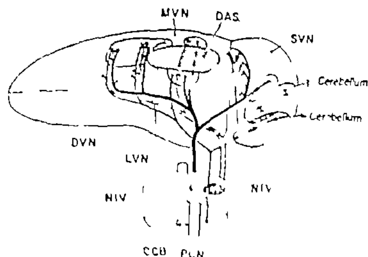


Fig. 48. Line drawing summarizing the central course and terminations of semicircular canal neurons in the vestibular nuclei. (See text for explanation of different sized lines.)

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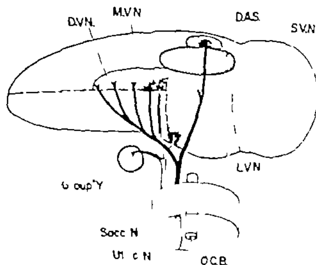


Fig 47 Line drawing summarizing the central course and termination of neurons supplying the otolith end organs.

ocular response to semicircular canal stimulation whether it be thermal (caloric) or rotational (post rotatory) At this endpoint histological examination has demonstrated a significant number of remaining hair cells in the cristae It has also been shown by electronmicroscopy that streptomycin affects type I hair cells before type II cells (Wersäll & Hawkins, 1962 Spoendlin 1966)

Maculae The vestibular neurons from the utricular and saccular maculae comprised the caudal part of the incoming vestibular root In so doing they showed striking differences from canal fibers with regard to termination (Fig 47) The macular fibers did not have terminals on the interstitial nucleus of the vestibular root (nor on similarly located neurons in the root) and they did not send ascending branches up to the SVN The utricular afferents did terminate on cells in the ventral LVN

The neurons of the utricular nerve appeared to be mainly small fibers with a smaller number of large fibers scattered evenly throughout The ascending rami of the utricular neurons passed through the rostro-ventral portion of the LVN In doing so they terminated on a surprisingly small number of medium to large neurons in this nucleus The main destination of these ascending rami appeared to be the rostral part (adjacent to the LVN) of the MVN The influence of the utricular macula on upper spinal cord muscle reflexes (by way of the rostro-ventral LVN) and the mediation through the MVN of compensatory eye movements form utricular stimulation may be emphasized by these connections. The descending branches of the utricular neurons appeared to converge in the rostral medial part of the DVN in the same area as the descending branches from canal fibers This appeared to be an area where all the vestibular endorgans (and cerebellum) converged on a relatively limited area in the vestibular nuclear complex and perhaps on the same neurons.

The saccular projection was the most unique of the vestibular endorgans. Analysis of the saccular nerve revealed that it is comprised predominantly of small fibers with fewer large fibers being present moreover numerically it was the smallest of the vestibular branches (Gacek & Rasmussen 1961) The saccular fibers were the most dorsal and caudal of all vestibular root fibers. Although the short descending branches converged on the rostral DVN area and a very small part of the ventral LVN the outstanding projection was that of the ascending branches. These terminated in the small group of cells called group "y" by Brodal This cell group was described previously by others (Fuse 1912) and does not appear to belong to the classical cerebellar or vestibular nuclei.

Indications are from the long controversy over the function of the saccule and from the fact that a definite function has never been clearly demonstrated, that the saccule is a special case in the physiology of vestibular endorgans. Anatomical support for this is provided by this unique projection to the group "y" nucleus

Value of physiological study of vestibular labyrinth

As stated in the introduction of this report, this study was undertaken to provide anatomical data of use to the neuro-physiologist. Most experiments on the function of different vestibular endorgans have involved the opening of the labyrinth itself which introduces an unknown but significant factor on all endorgans. With the operative approach and anatomical data presented in this study it is hoped that the proper physiological study can be designed and carried out to elucidate the function and basic neuro-physiology of not only the specific vestibular endorgans but hopefully different functional units within an endorgan.

SUMMARY

The course and central termination of first order bipolar neurons from the vestibular sense organs was determined in the cat. Wallerian degeneration of the central and peripheral axons of cell bodies injured by small lesions in Scarpa ganglion was demonstrated by the Nauta silver and the Sudan black B techniques. Reconstruction of the lesions and degeneration patterns in forty-seven animals revealed the following

1 Regardless of the peripheral location of the semicircular canal ampullae the central processes of all neurons supplying the cristae comprised the rostral two-thirds of the vestibular nerve and root the neurons innervating the maculae made up the remaining caudal portion of the nerve

2. Neurons from the cristae terminated by means of short collaterals in the interstitial nucleus of the vestibular root, then proceeded into the brainstem

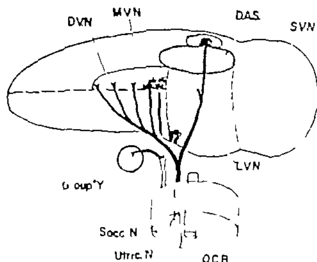


Fig 47 Line drawing summarizing the central course and termination of neurons supplying the otolith end organ

ocular response to semicircular canal stimulation whether it be thermal (caloric) or rotational (post rotatory) At this endpoint histological examination has demonstrated a significant number of remaining hair cells in the cristae It has also been shown by electronmicroscopy that streptomycin affects type I hair cells before type II cells (Wersall & Hawkins 1962 Spoendlin 1966)

Maculae The vestibular neurons from the utricular and saccular maculae comprised the caudal part of the incoming vestibular root In so doing they showed striking differences from canal fibers with regard to termination (Fig 47) The macular fibers did not have terminals on the interstitial nucleus of the vestibular root (nor on similarly located neurons in the root) and they did not send ascending branches up to the SVN The utricular afferents did terminate on cells in the ventral LVN

The neurons of the utricular nerve appeared to be mainly small fibers with a smaller number of large fibers scattered evenly throughout The ascending rami of the utricular neurons passed through the rostro-ventral portion of the LVN In doing so they terminated on a surprisingly small number of medium to large neurons in this nucleus The main destination of these ascending rami appeared to be the rostral part (adjacent to the LVN) of the MVN The influence of the utricular macula on upper spinal cord muscle reflexes (by way of the rostro-ventral LVN) and the mediation through the MVN of compensatory eye movements form utricular stimulation may be emphasized by these connections The descending branches of the utricular neurons appeared to converge in the rostral medial part of the DVN in the same area as the *descending branches from canal fibers* This appeared to be an area where all the vestibular endorgans (and cerebellum) converged on a relatively limited area in the vestibular nuclear complex and perhaps on the same neurons

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where each axon bifurcated into an ascending and a descending branch The ascending branches terminated in the superior vestibular nucleus and the cerebellum while the descending branches travelled in the vestibular root and gave off collaterals passing medially into the lateral medial and descending vestibular nuclei

A separate central localization was found for neurons supplying the posterior canal crista as opposed to those supplying the cristae of the superior vestibular division canals (superior and horizontal) This was particularly evident in the interstitial nucleus of the vestibular root the superior vestibular nucleus and the descending vestibular root and nucleus.

3 Neurons from the maculae did not terminate in the interstitial nucleus of the vestibular root or the superior vestibular nucleus. The ascending branches of the utricular neurons terminated in the rostro-ventral lateral vestibular nucleus and the rostral medial vestibular nucleus, while the descending branches gave off collaterals to the caudal medial vestibular nucleus and rostral descending vestibular nucleus. The central termination of saccular neurons was located mainly in the group "y" nucleus (Brodal) and to a lesser extent in the lateral and descending vestibular nuclei

4 In the superior vestibular nucleus the large caliber neurons from the superior division cristae terminated around the large cells in the center of the nucleus while the small diameter neurons from these endorgans ended peripherally in the nucleus where small cells predominate Such findings indicate different functional properties for the type I and type II vestibular hair cells. Large and small diameter nerve fibers were also found in all the vestibular nerve branches.

These anatomical data are presented to aid physiological study of the vestibular labyrinth and the first order neuron

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...logical structure of the ...seems to vary uncertainly ...d facts.

(M. Lawrence, [illegible])

...all classes to limited number ...al fact can serve as evidence ...al factors. Nature can reach ...according to very different ways.

(F. Mueller, [illegible])

Acta

OTO LARYNGOLOGICA

S U P P L E M E N T U M 253

LABYRINTHINE OTOSCLEROSIS

GEORGE KELEMEN

FRED H. LINTHICUM, JR.

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Acta

OTO LARYNGOLOGICA

S U P P L E M E N T U M 153

LABYRINTHINE OTOSCLEROSIS

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ACTA OTO LARYNGOLOGICA [illegible]

ACTA OTO LARYNGOLOGICA

SUPPLEMENTUM 253

From the Los Angeles Foundation of Otology and the School of Medicine,
University of Southern California, Los Angeles, California, U.S.A.

LABYRINTHINE OTOSCLEROSIS

GEORGE KELEMEN M.D.
FRED H. LINTHICUM, JR., M.D.

Emeritus Clinical Professor of Surgery (Otology) University of Southern California.
Associate Clinical Professor of Surgery (Otology) University of Southern California.

[illegible] interpretation of the physiological activities of the inner ear the number of theories seems to vary inversely with the number of established facts.

(M. LAWRENCE, [illegible])

[illegible] to react are given all tissues in limited number; the identical morphological fact can serve as evidence of very different etiological factors. Nature can reach the same end result, proceeding in very different ways

(F. M. [illegible], [illegible])

UPPSALA 1969

Supported in part by grant from the National Institute of Neurological Diseases and Blindness; the American Otological Society; and the Deafness Research Foundation.

Present address 130 West Third Street, Los Angeles, California 90057 U.S.A.

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CONTENTS

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1 INTRODUCTION

In the year 1899 Siebenmann spoke of "parallel features" as the result of his examination of hearing function one part corresponded to the stapedial ankylosi while the other presented an atypical picture in the form of a progressive nerve deafness. According to Siebenmann this duality was previously observed by Troeltsch (1858) but as the latter did not have any knowledge about otosclerosis, it is Siebenmann who designed labyrinthine otosclerosis" as a clinical entity Some of the terms applied later to the condition have been active capsular otosclerosis, cochlear type retrofenestral otosclerosis and perceptive hearing loss without stapedial ankylosis.

Krepuska and Krepuska (1936) pointed out that deafness can be the result of osseous changes in the cochlear capsule without stapedial ankylosi but it is not possible to separate labyrinthine deafness of this kind from others of inner ear origin without histologic evidence Sixty years after Si benmann s first description, Shambaugh (1959) still wrote that, ther than microscopic examination of the temporal bone there was no reliable method for diagnosing "pure labyrinth affection Seven years later H ople (1960) felt that cochlear otosclerosis might be the greatest single cause of nerve deafness. Lack of hist logical material may lead to different opinions Bosatra (1960) con idered otosclerosis of the inner ear as uncommon

Few f many talisiles will be quoted Fleischer (1962) studied the collection f Lange among about 1600 histological series of temporal bones he found 99 with otosclerosis, localized in 27 cases around the round window probably in lieating contact between the cochlear capsule and the otosclerotic focus. The material of Culld (1944) revealed 40 patients with histologic tosclerosi cont ct between cochlear capsule and otosclerotic focus occurred in 1 He declared that foci in independent reas in superior anterior or inferior part of the cochlear capsule rarely grow to a ize large enough to affect the hearing Such anatomic discrepancy with our findings I one of the evidences f different material, selected on ba is of surgical indications or not selected at all. Whether tabulated a one or the other it is obvi us that cochlear inv d ement i far from being a rarity Nylén (1949) was one among thers t emphasize the frequency of inv sion of the capsule of the l byrinth.

Further di cu ion of otosclerosis within the otic capsule a extant in our collecti n will be discu sed later in this paper

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Further discu ion f otosclerosis within the otic capsule as extant in our collection will be discu sed l ter in this paper

2 MATERIAL AND METHODS

At the present time there are 50 documented cases in our series. In three instances otosclerosis is unilateral. Besides this material now processed in sectional series, another group of about the same number is, at the present time, in different stages of histological processing. There were 24 males and 26 females. Ages varied between 45 and 83 years.

All represent "surgical" cases: either operated or the opposite unoperated side, or destined for operation which for some reason was not performed. Consequently the *material is of a very special nature comprising only* instances where the disease caused severe enough hearing loss for which the patient sought help.

Statistical evaluation has not been attempted for two reasons: *(1)* the group of temporal bones was not characteristic for otosclerosis in general; (2) the number of processed cases is continuously increasing and the tabulation would have to be repeatedly changed by addition of new data. No attempt is made to compare our figures statistically with data originating from other sources.

Because this study is looking for the anatomical basis of hearing loss due to otosclerosis, attention has centered on those cases showing contact between the cochlear capsule and otosclerotic focus. Among the 50 cases, 27 showed bilateral and 16 unilateral contact. This amounts to 86 percent, certainly a somewhat unexpectedly high proportion, explained by the method of obtaining temporal bones by the Los Angeles Foundation of Otology: the specimens have come from individuals with a progressive affliction.

According to the special aims of this study, changes *around the stapedial* footplate were not considered except as part of the analysis of the cochlear labyrinthine change.

A number of otosclerotic temporal bones outside this series served as an addition to the evaluation. However, they are not described and are not illustrated in this study. There were a number of points of interest in this group that have been used for comparison. Obviously not all the questions of relevance could be discussed.

Technically the use of wire prostheses created a particular problem in temporal bone processing. The difficulty was circumvented by determining by X-ray the exact position of the wire within the temporal bone, which was then sectioned in a plane *dictated by the orientation* of the embedded prosthesis. When the wire was reached, the celloidin block was inverted and sectioned starting from the bottom. Thus comparatively few sections

are lost The slice containing the wire can then be studied as an entity including photography

A factor of primary importance is preservation of the temporal bone which may have been obtained after several days of delay Early embalming at the mortuary is a distinct help in preserving soft tissues.

Experience has shown that the sensory structures, especially the organ of Corti, do not show a stage of preservation parallel with the condition of the entire body A cadaver in state of high decay may contain an intact Corti organ on the other hand, bodies obtained under comparatively favorable conditions may present a flat row of cells.

Lately decalcification by acid has been replaced by the versene technique as adapted for the temporal bone by Gussen and Donahue (1965) By this method the often vexing problem of overdecalcification can be safely avoided

The relative condition of the single elements within the temporal bone should command selective evaluation of the findings in the different tissues. The accuracy with which the delicate sensory organs, seen under the microscope can be evaluated has been doubted by some since the beginning of histological examination. This was re-emphasized as late as 1966 by Altmann, who warned that histological methods presently available for human temporal bones are often inadequate to establish beyond a doubt their intra vital nature Boundless confidence in the perfection of an individual's own preparation has been the origin of more than one assumption, or even general theory regarding function of the normal and the pathological cochlea and vestibulum

Involvement of the *carotid canal* (Fig 3) was infrequent. It took the form of a more or less wide protrusion replacing the wall for a generally short stretch. Significant deformation of the canal did not occur In one case a large fibrous resorption island within the focus opened directly into the canal.

Penetration of parts of the capsular wall of the *vestibulum* did not change the configuration of the saccular or the utricular maculae (Figs. 4 5) Cristae including cupulae showed their well known resistance compared to the condition of the organ of Corti.

Assault on the *semicircular canals* was not frequently seen The section of the bony canal was partly (Fig. 6) or completely transformed. *Once the entire circumference was formed by otosclerotic bone* this case was one of the very few where the involvement reached the tegmen over the labyrinth, under an unharmed dura. Some examples show complete encircling of the lumen of the horizontal canal at the site of a fenestration operation The mechanism of penetration at the canal wall is identical with that to be described in detail for the cochlear capsule the metaplastic process advances to the endosteum with a resulting contour deformity Typical rosary formation (see below) is seen, the fragmented particles taking the shape of vacuoles in a continuous row





Fig 1 Prom nt rv e l rged l y toselerotic appositi n 15

Fig. 2 J cobson s nerve d toselerotl focus. 40





Fig. 3. Focus reaching the bony wall of the carotid canal. 12.5.
Fig. 4. Focus in the base of the macula sacculi. 30.



Fig 1 Prom t rv nl rged by tosclerotic pposition. 15

Fig. 2 J cobson s rve a d otoscl roti focus. 40

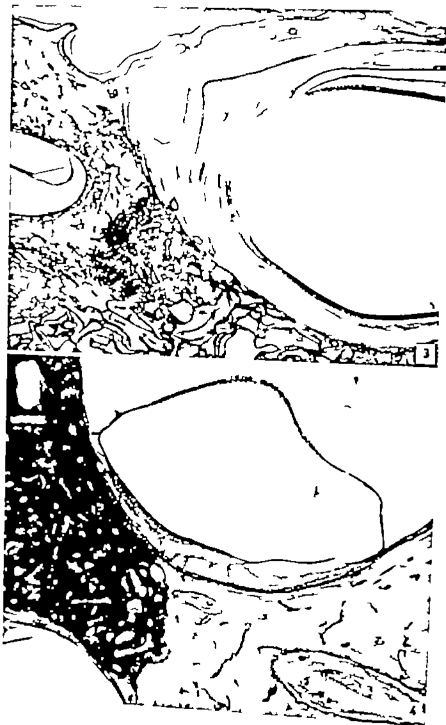


Fig. 3. Focus reaching the bony wall of the carotid canal 12.5.

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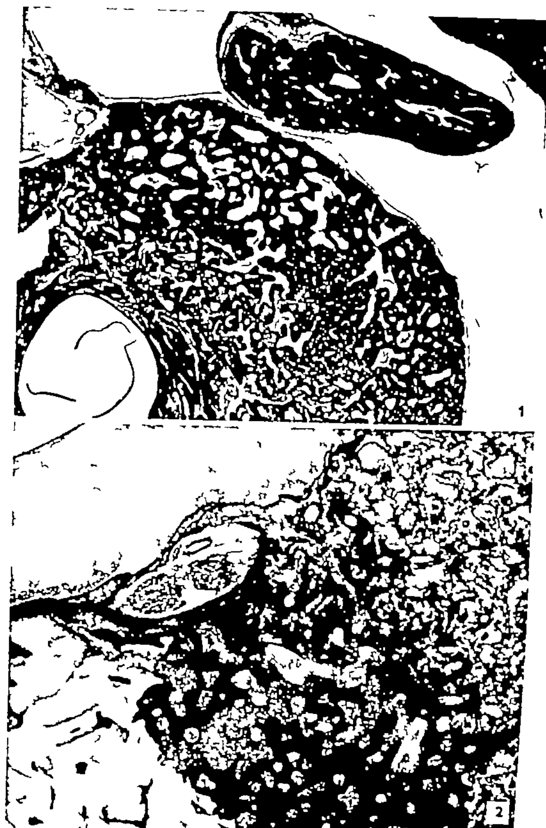


Fig 1 Prom t ry nlarged by t scl roti ppo iti 15

Fig 2. J cobso ers n d t sclerotl focus. 40





Fig. 7. Fissure (congenital?) in typical location between niche of round window membrane and base of the posterior crista (typical content). 45.

Fig. 8. Crack in the still-not-penetrated endosteal layer by pressure of the approaching otosclerotic mass. 110.

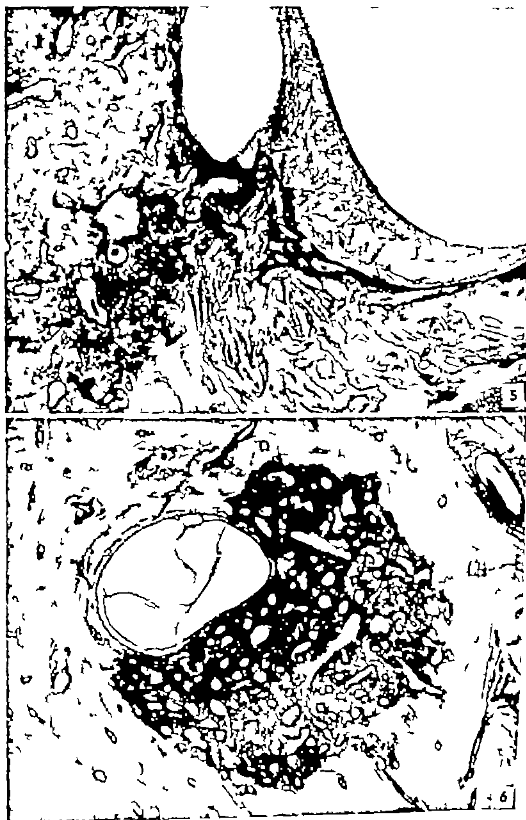


Fig 5 Ot l ro i In th cribriform pl te f the macul tricull 45.

Fig 6 Foc penetrati g the do t l l yer f the semicircula anal 55

3 HISTOPATHOLOGICAL FINDINGS

Involvement of the *middle ear* occurred in the form of a deeper protrusion of the promontory (Fig. 1) and a narrowing of the tympanic lumen. Where otosclerosis bone reached the lumen of the middle ear the wall lost its smoothness, but the "rosary" caused by fragmentation (see below) was absent, as there is no endosteal layer at this side Only a slight degree of engorgement was present in the covering mucosa Schwartze s sign could hardly be observed in these cases. In a temporal bone showing otosclerosis elsewhere a multilocular cyst protruded from the epitympanum while smaller exostoses formed under the tympanic mucous membrane

No instances were observed where the tissue of the *large ossicles* under went otosclerotic changes. Their normal, endless variance as to structure was present without any characteristic metaplasia.

Two nervous structures bounded by the middle and the inner ear respec tively are the nerve of Jacobson and the facial.

Instances of involvement of the *nerve of Jacobson* showed the canal, partly without compression of the nerve itself Fig. 2 shows the opening on the tympanic surface uninvolved. In other specimens the lamellae of the cortical bone succumbed to the attack. Another variant showed the roof of the canal transformed with part of the bottom free albeit finger like pro-tru ions testified to the approach of complete inclusion.

Replacement of the wall of the *facial canal* was the object of a separate study (Kelemen and Linthicum, 1965)

The otosclerotic focus advances by sheer physical force At the inner sur face of the bony capsule this shows in the form of cracks. The *endosteum* is burst open by the mass coming from the periphery (Fig. 8) The endosteum may remain intact but a crack appears in the endosteal bony layer indicating th approaching focus. These fissures are not to be confused with the crack around the otosclerotic focus which delimits it from the original capsular bone This is caused by different contraction coefficients in the fixation fluid, due to the *different* chemical composition of the two kinds of bone

The pressure will manifest itself as originating with finger-like processes protruding from the main mass of the focus, *singly* or in groups (Fig 9) The contour of the still intact capsular bone may be seen bulging before the pressure of the approaching *focus*. A protruding otosclerotic finger may p oceed bulkier parts of the focus, albeit the latter has already partially replaced the endosteum and has *initiated* destruction. On one occasion a proliferating finger was seen advancing *parallel* to the capsular wall.

Considering the localization of the always sharp boundary between the

No case was observed with involvement of the immediate surroundings of the *vestibular aqueduct* Several cases showed the *congenital fissure* in its most typical location connecting the niche of the round window with the base of the posterior crista (Fig 7)

The primary concern of this investigation was the involvement of the *cochlear capsule* by otosclerosis Conversion of the capsular bone to otosclerosis has been studied in detail particularly as it relates to functional changes that might occur when the suspension mechanism of the basilar ligament is distorted

Because of our special interest the delicate structure of the tissue of the spiral ligament created a very involved problem

In the illustrations, the stain applied when not noted otherwise was hematoxylin-eosin

The histological work was done by Mrs Agnes Cherchian Ward H T (ASCP) and Mrs Ruth Gregory Creulach the microphotography by Mr Lloyd Matlovsky (Regarding processing of temporal bones s. Cherchian Ward, 1967)

Replacement of the *endosteum* is the last step in the progress of the focus against the cochlear lumen (Fig. 28). This process follows an essentially regular course. But it must be emphasized that pressure exerted by the advancing new bone established within the external layers of the capsule before the endosteum is reached may already manifest itself within the latter by the appearance of cracks (Fig. 29).

The most conspicuous phenomenon of replacement is a sequence which may be called *fragmentation*. The endosteal layer is broken up into small particles (Fig. 30) and the latter form a *rosary* (row of beads) before disappearing definitely under the advancing otosclerotic mass. The particles may assume the form of vacuoles (Fig. 31). The same may be observed where the otosclerotic mass surrounds a semicircular canal (Fig. 32). Sometimes it is h rd to decide whether this margin belongs to the transformed endosteal layer or to the invading bone. In the latter case the much wider meshes of the otosclerotic bone must have changed into smaller and remarkably uniform vacuoles. So interpreted, the rosary represents the initial form of resorption of the endosteal layer before definite replacement.

Fragmentation accomplished, the original smoothness of the osseous contour is definitely lost (Fig. 33). The particles of this mosaic layer remain until their disappearance at the area of contact with the terminal layers of the fibers of the spiral ligament (Fig. 34). When this phase ends, attachment of the spiral ligament to the concavity of the capsular wall will *never* be reestablished in its original firmness.

The *periosteum* (endosteum) may line, unbroken, the original bone as well as the transformed section. Or it may be destroyed providing access for the direct contact of the otosclerotic bone with the lumen of the *scalae*. Isolated fibers of the disintegrating preiosteum produce a frayed border (Figs. 34, 35, 36).

This transformation of the attachment of the spiral ligament, and with it of the basilar membrane into otosclerotic bone is of prime importance. The three layers of the ligament as detailed by Neubert (1950, see below) remain recognizable but frequently with garbled boundaries, as the layers are permeated by cysts. Regarding the latter it is not certain whether they represent artifacts in this conglomerate of loose fibers which may change their position during fixation, similar to that which happens to Reissner's membrane.

In many cases, the dense external layer of the ligament was well represented, but compressed by the advancing new bone. This resulted in considerable deformation of the capsular contour. Edematous inhibition, a result of vascular damage by the otosclerotic penetration, produced a more even picture of the spiral ligament after obliteration of the normal differentiation of its layers. By this mechanism larger cysts are created. Instructive pictures appear where the dense external layer of the ligament, hardly distinguishable from the periosteum, meets the fragmented endosteal bone: the fibers of the ligament still penetrate the broken-up bone adjacent to it.

original bone and the focus progressing toward the cochlear lumen one has to distinguish between comparatively mute areas, lying outside the area of attachment of the spiral ligament and functionally significant ones covering partially or totally the area behind the latter

Contour changes within the cochlea varied markedly from mild flattening of the concave walls to gross alteration with narrowing of the lumen and the occurrence of protuberances in form of exostoses The concave contour may assume an angulated shape Angulations may become critical when developed behind the anchorage of the basilar membrane (Fig 10) A high degree of deformity transformed the scala tympani into a funnel shaped space (Fig 11) In some instances the entire wall seemed to advance while nearby the protrusion assumes the character of an exostosis (Figs. 12, 13, 14)

In two cases, in contact with the otosclerotic focus, non-otosclerotic bone filled the tympanic scala of the basal turn (Figs 15 16, 17 18) In another case of labyrinthic invasion by otosclerosis, non-otosclerotic bone filled the perilymphatic space of the horizontal canal (Fig 19)

The cochlear contours can be altered on occasions by penetration of otosclerotic bone into *interscalar septa* with resultant endosteal destruction (Fig 20) Progression through the interscalar septum may reach the modiolus

In the region of the *round window* the membrane can be involved in several ways The shape of the annulus may be altered (Fig 21) at the cochlear aspect of the membrane A lamina of otosclerotic bone can form a duplication (Fig 22) The window may be bridged over by a mass which totally buries the membrane and protrudes into the niche transforming the latter into a narrow cavity (Fig 23)

The cochlear orifice of the *cochlear aqueduct* was found in some instances *completely surrounded* by otosclerotic bone which accompanied the duct along a portion of its course No complete closure was observed One case (with a dilated cochlear orifice) without otosclerotic bone in the immediate vicinity but present elsewhere in the cochlear capsule showed the endothelial membrane continuing unbroken over the orifice as described by Wallner (1947)

The newly established otosclerotic wall of the scalae may respect the original contour but rather than smooth is wavy in a high or moderate degree (Figs 24 25) Resorption cavities inside the focus are by a fibrous network frequently reach the inner surface either in a silent" "mute region or over the spiral ligament (Fig 26) An entire system of similar spaces may form in series (Fig 27)

Evaluation of the mechanism by which spongiotic or sclerotic bone reached the cochlear capsule did not give any clear-cut results, but certainly is worth further investigation Either one or the other kind of metaplastic bone advanced against the capsule or both participated in the attack.

Otosclerotic foci of the so-called burnt out" character are extant in our collection, but no example presented itself within the series here discussed

Replacement of the *endosteum* is the last step in the progress of the focus against the cochlear lumen (Fig 28) This process follows an essentially regular course. But it must be emphasized that pressure exerted by the advancing new bone established within the external layers of the capsule before the endosteum is reached may already manifest itself within the latter by the appearance of cracks (Fig 29)

The most conspicuous phenomenon of replacement is a sequence which may be called *fragmentation* The endosteal layer is broken up into small particles (Fig 30) and the latter form a *rosary* (row of beads) before disappearing definitely under the advancing otosel rotic mass. The particles may assume the form of vacuoles (Fig 31) The same may be observed where the otosclerotic mass surrounds a semicircular canal (Fig 32) Sometimes it is hard to decide whether this margin belongs to the transformed endosteal layer or to the invading bone. In the latter case, the much wider meshes of the otosclerotic bone must have changed into smaller and remark ably uniform vacuoles. So interpreted, the rosary represents the initial form of resorption of the endosteal layer before definite replacement.

Fragmentation accomplished, the original smoothness of the osseous contour is definitely lost (Fig 33) The particles of this mosaic layer remain until their disappearance at the area of contact with the terminal layers of the fibers of the spiral ligament (Fig. 34) When this phase ends, attachment of the spiral ligament to the concavity of the capsular wall will never be reestablished in its original firmness.

The *periosteum* (endosteum) may line unbroken, the original bone as well as the transformed section Or it may be destroyed providing access for the direct contact of the otosclerotic bone with the lumen of the scalae. Isolated fibers of the disintegrating preiosteum produce a frayed border (Figs. 34 35 36)

This transformation of the attachment of the spiral ligament, and with it of the basilar membrane into otosclerotic bone is of prime importance. The three layers of the ligament as detailed by Neubert (1950 see below) remain recognizable but frequently with garbled boundaries, as the layers are permeated by cysts. Regarding the latter it is not certain whether they represent artifacts in this conglomerate of loose fibers which may change their position during fixati n, similar to that which happens to Reissner's membrane

In many cases, the dense external layer of the ligament was well represented, but compressed by the advancing new bone. This resulted in considerable deformation of the capsular contour Edematous inbibition, a result f vascular damage by the otosclerotic penetration, produced a more even picture of the spiral ligament after obliteration of the normal differentiation of its layers. By this mechanism larger cysts are created. Instructive pictures appear where the dense external layer of the ligament, hardly di tinguishable from the periosteum, meets the fragmented endosteal bone the fibers of the ligament still penetrate the broken-up bone adjacent to it.





Fig 9 Otosclerotic "fl gers" f fro tal attack g l t th l mella of the origi al bone (G mori impregnation) 220

Fig 10 Co t ur def rmati n f the capsular wall with loosening f the ba il mem bran by the spongi us focus. 75



Fig. 11. Considerable deformation of the contour of the cochlear capsule withi[illegible] rea of the focus. 22×.

Fig. 12. Otosclerotic protrusions in the tympanic scala of the basal turn. 75×.





Fig 13 Otosclerotic protrusion near the cribriform lamina 20

Fig 14 Otosclerotic protrusion into the tympanic scala of the basal turn 20





Fig. 15. Otosclerotic bone of the cribriform lamina; non-otosclerotic bone in the scala tympani of the basal turn. ×32.

Fig. 16. Otosclerotic bone in the tympanic scala of the basal turn (Mallory Heidenhain) ×20.





Fig 17 N n-ot sclerotic new bone in the tympa ic se l f th basal t rn, dj cent t an tosel roti focu l th caps l 30

Fig 18. Ot scl rotic bo rrou ding the basal turn, with no -otosclerotl new bon i th modi l 12.

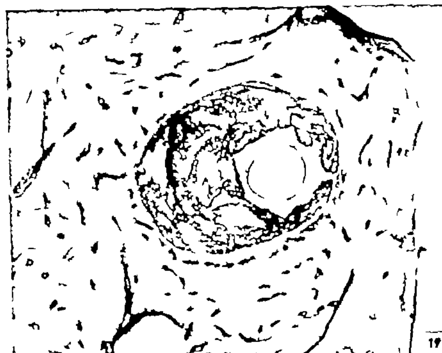




Fig. 19. Otosclerotic bone fill[illegible] g the perilymph space i the semicircular canal, lea ing the endolymphatic tube free 35.

Fig. 20 Focus penetrating the intercalar septum. 35.



Fig 17 \ n-ot sclerotic new bon I the tymp I scala of th basal turn, adj ce t to n ot sclerotl focu I the capsul ×30

Fig 18 Ot scl rotic bo urro di g the basal t rn, with -otosclerotl new bone in the modi l 12.

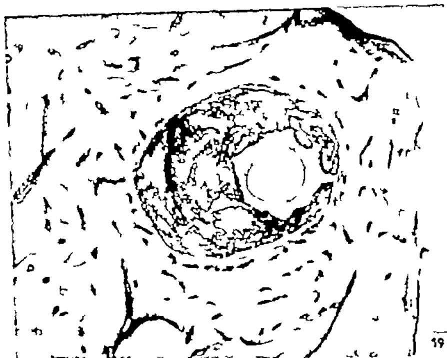




Fig. 19. Otosclerotic bone filling the perilymph space of the semicircular canal, leaving the endolymphatic tube free. 35

Fig. 20. Focus penetrating the interscala septum. 35.



Fig 21 Otosclerotic framl g f the membrane f th round wi d w 55

Fig 22. Otosclerotl co er f th m mbra of th ro nd wind w 33





Fig. 23. Replacement of the membrane of the round window by the otosclerotic mass. ×32.

Fig. 24. Penetration of endosteal layer by the focus. ×35



Fig. 21. Otosclerotic "framing" of the membrane of the round window. ×55

Fig. 22. Otosclerotic cover of the membrane of the round window. ×33

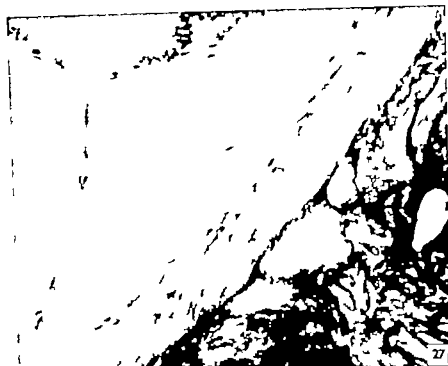




Fig. 27. Row of marrow spaces in contact with the endosteum. 220.

Fig. 28. Protrusions of the focus into the endosteal layer. 125



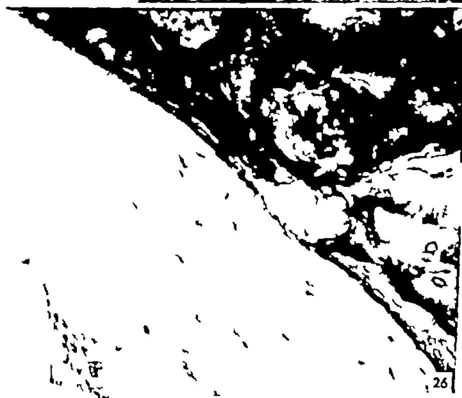


Fig 25 R pl cement f th nd st 1 l e th focu re hing th lost m 125

Fig 26 Larg m rrow pace re hi g th d t um 275

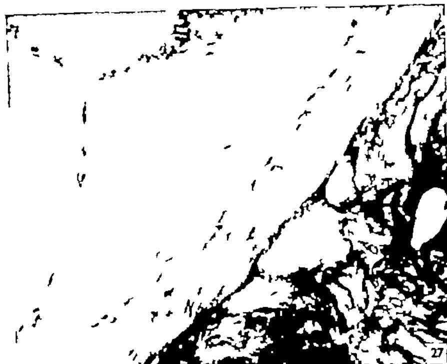
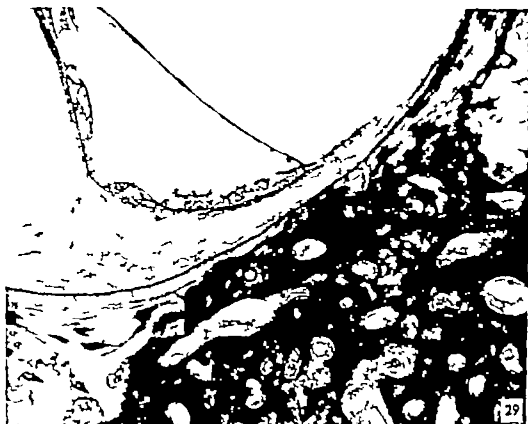




Fig. 27. Row of marrow spaces in contact with the endosteum. 220

Fig. 28. Protrusions of the focus into the endosteal layer 125



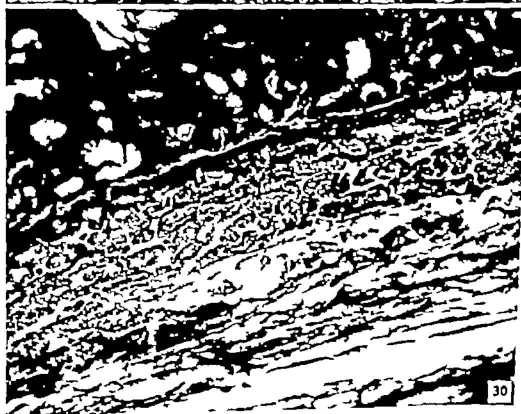


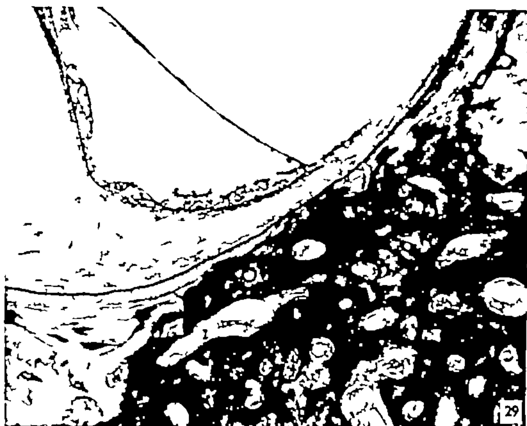
Fig 29 P t tl f th endost al l er dl l tegratl f the scala tria 75

Fig 30. Fragm nt tl n f th endost al la dlsl l gration f th fibers of the piral lig ment 500



Fig. 31. Fragmentation of the endosteal layer: vacuoles among the fibers of the spiral ligament. 115

Fig. 32. Fragmentation in the endosteal layer of semicircular canal, surrounded by the focus. 33.



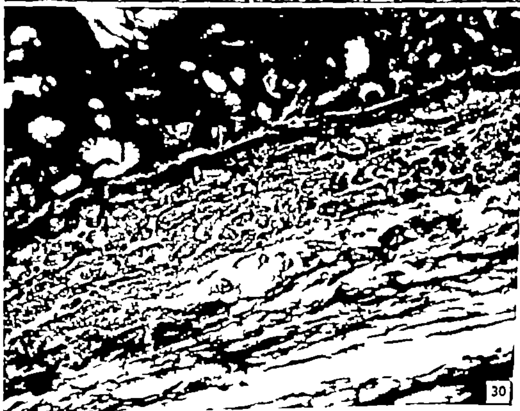


Fig 29 Penetrati n f th ndosteal l yer di l t grati f the scul t l 75

Fig 30 Fragm nt ti n f th nd t l l yer di l t grati f th fibers of the piral ligame t 500



Fig 35. "Fraying" at the edge of the spiral ligament (Gomori impregnation) 250

Fig 36 "Fraying" of the disintegrating periosteum. 250.



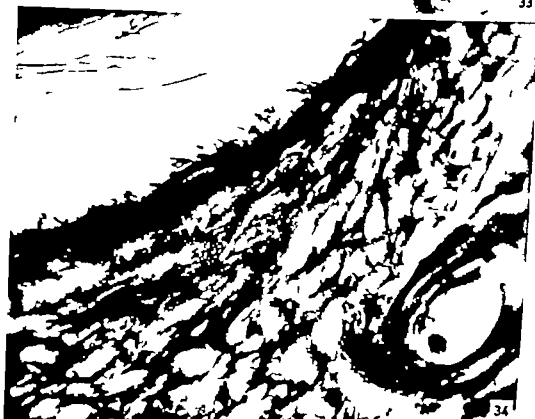


Fig 33 Fragm t tl with acu l f rmati n f th dosteal l y dl l tegrati n f the dosteum. 135

Fig 34 Dl l tegrati with "fra l g f the fibe n tw k of the piral lig me t 480



Fig. 39 Focus at the isthmus of the internal meatus. 20

Fig. 40. [illegible] focus with [illegible] engorgement, harboring large resorption space 22.

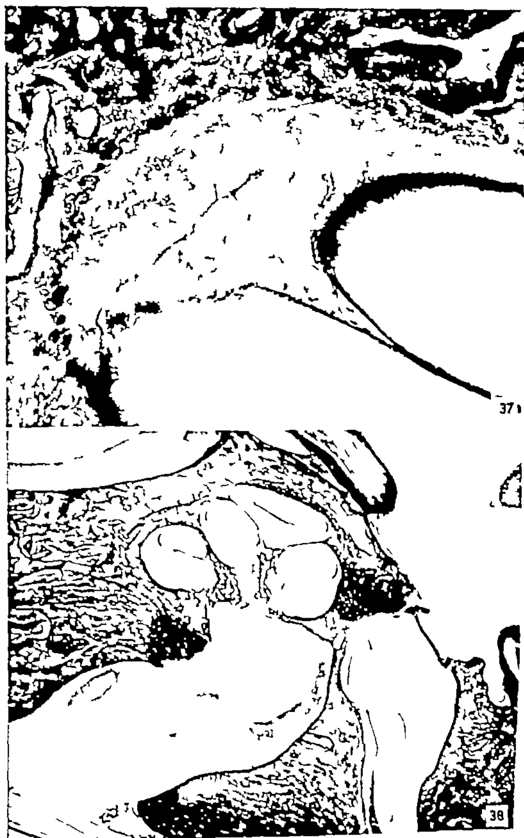


Fig 37 Fragm ntation, rosary lik of the nd teal l yer Irregular loose ing of th fibrou network of the piral ligam t 75

Fig 38 Focu at the isthmu f the l tern l m t x 6



Fig. 39. Focus [illegible] the [illegible] the internal meat[illegible]. × 20

Fig. 40. [illegible] focus with [illegible] engorgement, harboring larg[illegible] resorption space × 35.





Fig 41 Wall f l tern l m t s. Large resorpti pace surrou ded b th focu nd connected with the lumen f th meatus. 17.5

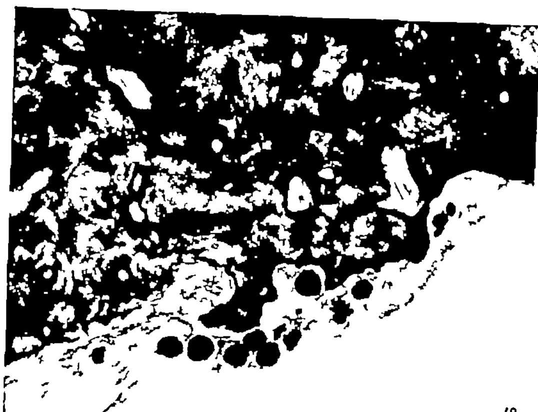
Fig 42 Otoscl rotic crescences betwee th fibers f the VIII n 23



Fig. 43. Focus at the base of the cochlea, harbori[illegible] [illegible]ide resorption [illegible]pace with exostosis. 15

Fig. 44. Non-otosclerotic exostoses in the inner meat[illegible] [illegible] case with otosclerosis else-where [illegible] 38.

3 [illegible] Kelemen



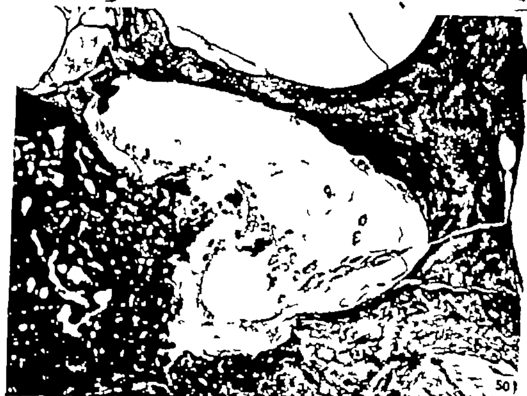


Fig 49 I meat l t f psamm m am ng the nfractu ities f th focus. 75

Fig 50 Inn r meat focus, protrudi g with pl es, a d cluster f psamm mas. 223





Fig. 51. Inner meat[illegible] gl[illegible] psammoma [illegible]ith osteoblast[illegible] × 250

Fig. 52. Protru[illegible]ion of the focus int[illegible] the endosteal la[illegible]er. Tabl[illegible] 103 *of the* [illegible] of P[illegible] Ma[illegible] 1917



53

Figs. 53 nd 54 (A B C, D) Ex mples of m imal I lv ment f the cochl ar c p ul by the tosclerotl process.

In some cases there is a seperation of the two (as e g Fig 37) Warping of the basilar membrane as it enters the apex of the spiral ligament depends too much on the hazards of the histological processing to represent condi tions in vivo



54

The same skepticism must prevail regarding the *organ of Corti.* While in many instances its good preservation represents in vivo conditions, the rat of disintegration does not give reliable information regarding the status before death, i.e. damage done by post mortem changes.

Otosclerosis destruction in olving the *internal auditory canal* can be divided into three di tinct steps (1) Metaplasia reaches the walls of the



53

Figs. 53 and 54 (*A B C, D*) Examples f ma lm l l l ment f the cochl a p ule by the otoscleroti process.

In some cases there is a seperation of the two (as e g Fig 37) Warping of the basilar membrane as it enters the apex of the spiral ligament depends too much on the hazards of the histological processing to represent condi tions in vivo



34

The same skepticism must prevail regarding the organ of Corti. While in many instances its good preservation represents in vivo conditions, the rate of disintegration does not give reliable information regarding the status before death, i.e. damage done by post mortem changes.

Otosclerosis destruction involving the *internal auditory canal* can be divided into three distinct steps (1) Metaplasia reaches the walls of the

canal (2) New bone protrudes into the lumen of the canal (3) The 8th nerve is directly attacked by otosclerotic excrescences

1 The canal wall can show considerable masses of the new bone but, besides the breaking up of the originally smooth contour the lumen is fully conserved (Figs. 38 39) This form is infrequent as the focus generally penetrates deeper and causes more disorder

2 The new bone surrounds the canal narrowing it in a very irregular way (Figs 40 41 42) Into the center of a large resorption island, in a focus around the inner meatus, a spiny exostosis has grown (Fig 43) In other cases of otosclerosis, a non-otosclerotic exostosis grew into the inner meatus (Fig 44) Over the focus located in the wall of the inner meatus, the thickened dura was engorged Schwartze s phenomenon in this location

3 Direct attack against the 8th nerve took different forms Buckling inward of the newly formed mass caused deviation and stretching of the fibers (Fig 45) Sharper protrusions caused a more conspicuous kind in the nerve (Fig 46) Finally spine-like protrusions penetrated the trunk (Fig 47)

Potential danger to nerves by sharp bony spurs at their divisions (facial and chorda cochlear and vestibular branches of the 8th nerve in the inner meatus) was pointed out previously (Kelemen 1934)

No causal connection can be constructed between otosclerosis and *psammomas* in the dura of the inner meatus. However they were seen so often and so conspicuously distributed in intimate relation to otosclerotic foci that they should be mentioned here Long rows lined the walls in vicinity of the focus (Fig 48) They showed a predilection to nestle in the anfractuosities of a focus (Figs. 49 50) Some parallelism can be constructed for this predilectional location by their vascular origin and the above-mentioned engorgement over the otosclerotic focus. One giant specimen showed besides a lamellary cortex a small vessel in its center and even osteoblast like cortical seams (Fig 51) Here possibly not a single vessel but a small vascular conglomerate underwent the calcifying process.

Figs. 53 (*A B C D*) and 45 (*A B C D*) represent examples of maximal involvement of the cochlear capsule by the otosclerotic process.

Evaluation of several instances with non-otosclerotic lamellar bone filling the scala tympani in contact with the otosclerotic focus shall wait until more cases with comparable cases are obtained

4 AUDIOMETRIC CONSIDERATIONS

Several reports indicated in past years that there is no relationship between otosclerosis and sensori neural hearing loss (Guild, 1933 Feldman, 1960 Glorig and Gallo, 1962) However many clinicians with a large number of otosclerotic patients are convinced that a relationship does exist (Carhart, 1962, 1963 Shambaugh, 1964 Derlacki and Valvassori, 1965 House, 1966)

Continuing correlation of audiometric tests with histopathologic findings tends to indicate at the present time, that there exists a definite relationship

TABLE 1 *Age distribution of individuals with otosclerosis in the entire collection*

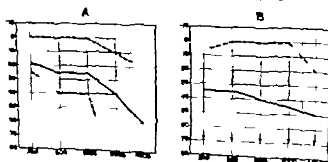
	Range	Average
Without cochlear involvement	47–[illegible]	66
With cochlear involvement	45–83	62

TABLE 2 A *Composite audiogram of the individuals in whom the lesion was limited to the footplate and vestibule*

The center dark line indicates the average bone conduction level of this group. The upper dotted line represents the BC level of the individual with the best threshold and the lower dotted line indicates the threshold of the patient with the poorest hearing. No individual in this group showed complete loss of bone conduction.

TABLE 2 B *Composite audiogram of the individuals in whom the otosclerotic lesion invaded the endosteal layer of the cochlear capsule*

The solid line represents the average bone conduction threshold in this group. The upper dotted line represents the threshold of the patient with the best BC level. The down-pointing arrows indicate that several patients had no measurable bone conduction. (BC thresholds converted to ISO standards.)



canal (2) New bone protrudes into the lumen of the canal (3) The 8th nerve is directly attacked by otosclerotic excrescences

1 The canal wall can show considerable masses of the new bone but besides the breaking up of the originally smooth contour the lumen is fully conserved (*Figs 38 39*) *This form is infrequent as the focus generally* penetrates deeper and causes more disorder

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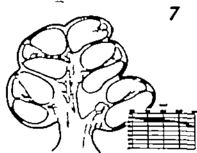
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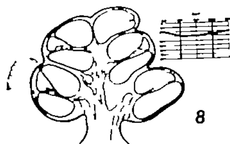
Figs 53 (*A B C D*) and 4) (*A B C D*) represent examples of maximal involvement of the cochlear capsule by the otosclerotic process.

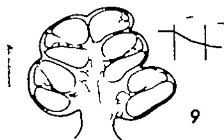
Evaluation of several instances with non-otosclerotic lamellar bone filling the scala tympani in contact with the otosclerotic focus shall wait until more cases with comparable cases are obtained

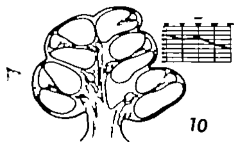
TABLE 4 *Schematic representation of the portion of the endosteum involved by otosclerosis with accompanying audiograms to show bone conduction thresholds as measured by ASA standards*

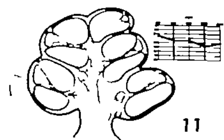
Note that in Case 7 the upper two coils but not the basilar turn are involved. The hearing in this case is good. Case 13 represents one of two cases in our series in which only the basilar turn was involved, and the BC threshold was considerably elevated.

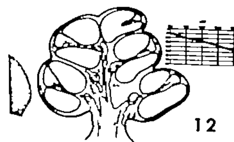












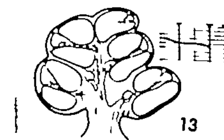
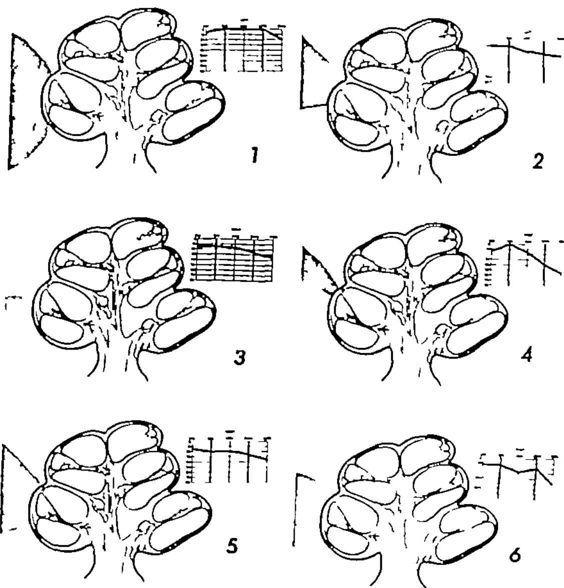


TABLE 3 *Schematic representation of the endosteum involved by otosclerosis with accompanying audiograms to show bone conduction thresholds as measured by ASA standards*

Note that only the basilar turn is involved and that the thresholds are all good.



Surgical attempts to correct the sensiro-neural loss, or prevent its progression have been made by W House (1962) According to the concept of Goodhill (1963) he opened the obliterated round window in several cases this failed to improve the hearing Suspecting that a massive otosclerotic lesion visible on X rays, might be constricting the internal auditory canal he also opened this through the middle fossa route These results likewise were not encouraging Recently he has attempted to improve the blood supply to the cochlea by thinning the cochlear capsule and transplanting it to the tensor tympani muscle (1967) This procedure was based on

TABLE 6. *Schematic representation of the portion of the endosteum involved by otosclerosis with accompanying audiograms to show bone conduction thresholds as measured by ASA standards*

Note that Case 20 is one of two in our series in which only the basilar coil is involved and the BC threshold is considerably elevated. Note that in Case 24, although the basilar coil is not involved, the internal auditory canal is.

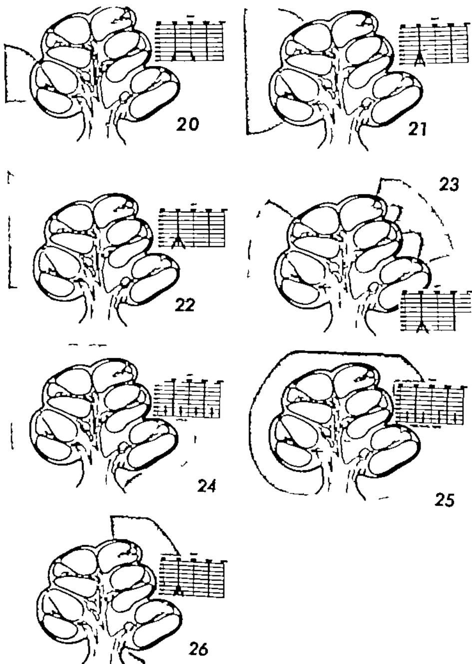
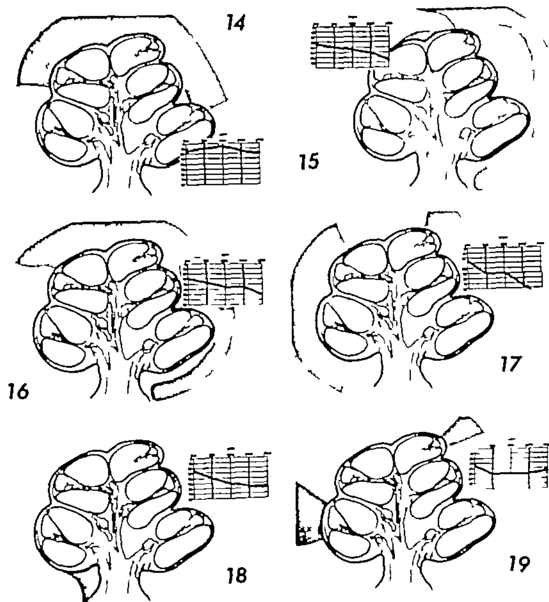


TABLE 5 *Schematic representation of the portion of the endosteum involved by otosclerosis with accompanying audiograms to show bone conduction thresholds as measured by AS 1 standards*

N t that either the ba ilar coil and one ther coil are inv lved, o there is invol ement of the internal audit ry canal All but Case 14 show a signific t increase in the BC threshold

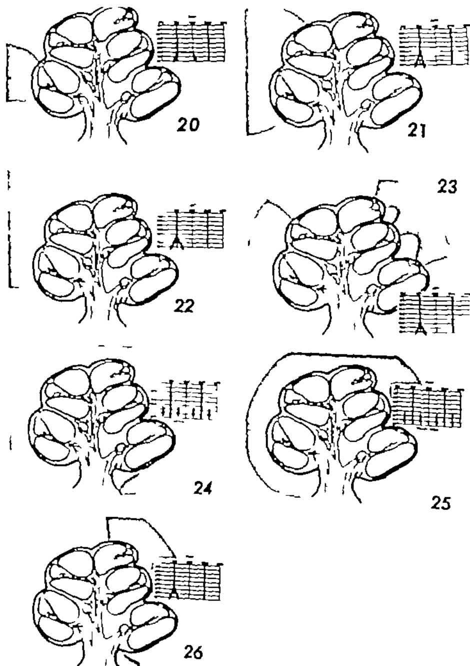


the findings of Rüedi (1965) who has reported vascular shunts between the spiral ligament and the otosclerotic focus Effectiveness of this attempt has yet to be determined as insufficient time has passed since the interven tion was carried out

To rule out presbycusis as a possible cause of increased loss in cases with cochlear involvement the ages were compared with those individuals with oval window otosclerosis but no cochlear involvement (Table 1) It was found that the age spread was almost identical in the two groups, with

TABLE 6. *Schematic representation of the portion of the endosteum involved by otosclerosis with accompanying audiograms to show bone conduction thresholds as measured by ASA standards*

Note that Case 20 is one of two in our series in which only the basilar coil is involved and the BC threshold is considerably elevated. Note that in Case 26, although the basilar coil is not involved, the internal auditory canal is.



the average in the mid sixties The patient with the most extensive otosclerotic lesion and total absence of hearing was 54 years old (illustrations 24 and 25 in Table 6)

Table 2 shows composite audiograms comparing the bone conduction thresholds of individuals with otosclerosis limited to the footplate and vestibule and with those with cochlear otosclerosis

Comparison of these two composite audiograms indicates that the sensori neural loss in those individuals with involvement of the endosteal bony layer of the cochlea by otosclerosis is greater than in those in which the lesion is limited to the footplate and vestibule

An attempt was made to correlate the area of the cochlea involved by otosclerosis and the amount of hearing loss and configuration of the audiogram No pattern could be ascertained that produced a characteristic audiometric curve. It was noted however that if the basal coil of the cochlea plus one other coil or the internal auditory canal was involved by the otosclerosis, there was more apt to be a sensori neural loss (Tables 5 and 6) In observing Tables 3 and 4 it will be noted that in no case was the spiral ligament area of the basal coil plus one other coil involved These patients for the most part have relatively good bone conduction thresholds with the exception of case No 13 where it was depressed to 40 dB

If we examine case 14 through 26 (Tables 5 and 6) we find that in most of the cases the basal plus one or more other coil was involved by the otosclerosis. In all but one of these cases, the bone conduction level was considerably depressed An exception is case 18 in which the internal auditory canal alone was involved another exception is case 26, where the internal auditory canal plus the two apical turns were involved It would appear from these illustrations that if the basal turn and/or the internal auditory canal plus one or more of the other turns of the cochlea are involved there is more likely to be a sensori neural impairment

About half of the cases exhibited involvement by otosclerosis of the endosteal layer of the cochlea Correlation of the audiometric bone conduction tests *indicate that when there is endosteal layer involvement* there is more apt to be depression in the bone conduction threshold irrespective of the age of the patient

5 DISCUSSION

A panel discussion on sensori-neural deafness in otosclerosis at the American Otological Society (1966, *Annals of Otol Rhinol, Laryngol*) summarized the present status of the conception of labyrinthine, or cochlear otosclerosis. The 13 participants based their presentations, a total of 276 cases with 489 ears, partly on personal observations, partly on studies of extant collections.

Hansen and Reskie-Nielsen (1965) emphasized that the histological measures presently available for processing human temporal bones are often inadequate to establish, beyond doubt, their intravital correlates. Friedman (1968) pointed to the technical limitations when interpreting morphology. Osseous changes have been analyzed in detail in past years since Politzer (1892) described the pathologic entity of otosclerosis. The status of the sensory end organs has been more difficult to evaluate. Many of the descriptions of atrophic lesions have to be disregarded as representing merely the results of unsatisfactory preservation, due to delay between death and processing, and other factors. Imponderabilia played their role in the findings of the most distinguished observers. Lange (1926) pointed out that Wittmaack infrequently found pathological inner ears while Manasse saw them extraordinarily often.

In a preceding section hist pathological changes were described in single regions of the ear. The following survey correlates these findings with data of the literature.

The *middle ear* is infrequently discussed. It is always taken for granted that the metaplastic process is restricted to the bone of the otic capsule.

The *tegmen* was involved in our material in only one specimen by penetration from the direction of the superior semicircular canal. Malan (1940) observed foci in the tympanic tegmen.

Manasse (1917) enumerated the regions where otosclerosis oversteps the normal boundaries of capsular bone: tympanic cavity, membrane of the round window, inner acoustic meatus, and finally spaces inside the osseous labyrinth. The body of the temporal bone outside the otic capsule contains *congenital fissures*, brought into causal connection with the otosclerotic area (discussion see Kelemen, 1933). The most prominent run from the bottom of the niche of the round window to the base of the posterior crista. A number of these formations were seen in our material with no relation between the fissures and otosclerosis.

Politzer (1894) quoted the case of Katz and Habermann with osteoporotic changes in the head of the malleus, and in the body of the incus. The

the average in the mid sixties. The patient with the most extensive otosclerotic lesion and total absence of hearing was 54 years old (illustrations 24 and 25 in Table 6)

Table 2 shows composite audiograms comparing the bone conduction thresholds of individuals with otosclerosis limited to the footplate and vestibule and with those with cochlear otosclerosis

Comparison of these two composite audiograms indicates that the sensori neural loss in those individuals with involvement of the endosteal bony layer of the cochlea by otosclerosis is greater than in those in which the lesion is limited to the footplate and vestibule.

An attempt was made to correlate the area of the cochlea involved by otosclerosis and the amount of hearing loss and configuration of the audiogram No pattern could be ascertained that produced a characteristic audiometric curve It was noted however that if the basal coil of the cochlea, plus one other coil or the internal auditory canal was involved by the otosclerosis, there was more apt to be a sensori neural loss (Tables 5 and 6) In observing Tables 3 and 4 it will be noted that in no case was the spiral ligament area of the basal coil plus one other coil involved These patients for the most part have relatively good bone conduction thresholds with the exception of case No 13, where it was depressed to 40 dB

If we examine case 14 through 26 (Tables 5 and 6) we find that in most of the cases the basal plus one or more other coil was involved by the otosclerosis In all but one of these cases, the bone conduction level was considerably depressed An exception is case 18, in which the internal auditory canal alone was involved another exception is case 26 where the internal auditory canal plus the two apical turns were involved It would appear from these illustrations that if the basal turn and/or the internal auditory canal plus one or more of the other turns of the cochlea, are involved, there is more likely to be a sensori-neural impairment

About half of the cases exhibited involvement by otosclerosis of the endosteal layer of the cochlea Correlation of the audiometric bone conduction tests indicate that when there is endosteal layer involvement there is more apt to be depression in the bone conduction threshold, irrespective of the age of the patient

5 DISCUSSION

A panel discussion on sensori-neural deafness in otosclerosis at the American Otological Society (1966, *Annals of Otol Rhinol., Laryngol.*) summarized the present status of the conception of labyrinthine or cochlear otosclerosis. The 13 participants based their presentations, a total of 278 cases with 489 ears, partly on personal observations, partly on studies of extant collections.

Hansen and Reskie-Nielsen (1965) emphasized that the histological measures presently available for processing human temporal bones are often inadequate to establish, beyond doubt, their intravital correlates. Friedman (1968) pointed to the technical limitations when interpreting morphology. Osseous changes have been analyzed in detail in past years since Politzer (1892) described the pathologic entity of otosclerosis. The status of the sensory end organs has been more difficult to evaluate. Many of the descriptions of atrophic lesions have to be disregarded as representing merely the results of unsatisfactory preservation, due to delay between death and proceeding, and other factors. Imponderabilia played their role in the findings of the most distinguished observers. Lange (1926) pointed out that Wittmaack infrequently found pathological inner ears while Manasse saw them extraordinarily often.

In a preceding section histopathological changes were described in single regions of the ear. The following survey correlates these findings with data of the literature.

The middle ear i infrequently discussed. It is always taken for granted that the metaplastic process is restricted to the bone of the otic capsule.

The *tegmen* was involved in our material in only one specimen by penetration from the direction of the superior semicircular canal. Malan (1940) observed foci in the tympanic tegmen.

Manasse (1917) enumerated the regions where otosclerosis oversteps the normal boundaries of capsular bone: tympanic cavity, membrane of the round window, inner acoustic meatus, and finally spaces inside the osseous labyrinth. The body of the temporal bone outside the otic capsule contains *congenital fissures* brought into causal connection with the otosclerotic area (discussion see Kelemen, 1933). The most prominent run from the bottom of the niche of the round window to the base of the posterior crista. A number of these formations were seen in our material with no relation between the fissures and otosclerosis.

Politzer (1891) quoted the case of Katz and Habermann with osteoporotic changes in the head of the malleus, and in the body of the incus. The

large ossicles have been repeatedly described to be a site of otosclerotic changes These were not found in our material

Congenital stapes fixation (Kelemen 1943 Altmann 1949) causing labyrinthine hearing defects, was discussed by Shambaugh (1952) House House and Hildyard (1958) found cochlear involvement in some of these cases manifested predominantly in higher frequencies Richards (1964) *found this condition in a case with rubella*

Among the *nervous elements* the *nerve of Jacobson* seems to have been entirely disregarded as to a role in the hearing mechanism except indirectly as a source of tinnitus According to Lempert (1946) vascular changes on the promontory could be a source of ear noises. As no role in the hearing mechanism was assigned to this nerve cases where the walls of its canal were partly or completely transformed by otosclerosis are in this report simply enumerated

The relations of the *facial nerve* to otosclerotic foci were studied by Kelemen and Linthicum (1965) Jones (1941) was the only author who included participation of the facial into the otosclerotic syndrome declaring facial paralysis *a most notable symptom of the disease Never mentioned* before this finding was equally ignored after Jones publication

The most conspicuous picture of *vestibular participation* showed the osseous base of the end organs with their respective cribriform plates transformed to otosclerotic bone completely surrounding the nerve fibers. No blockage or even compression was seen under the microscope the functional aspect of the condition will be discussed below

Siebenmann (1899) arrived at the conclusion that participation of the canal of the utriculo-ampullar nerve in the metaplastic process leaves the nerves *and fibrous surroundings unaltered* with the ampulla remaining free of changes and without functional disturbance On the other hand he explained Menière attacks, in otosclerosis, by ruptures of partitions in the vestibule causing sudden changes in pressure and position This concept was taken up many decades later by several writers

Frequent incorporation of the cisternal wall in the otosclerotic focus makes the macula of the saccule eminently vulnerable

Ruttin (quoted by Ruedi Acta, 1964) indicated that vertigo may occur due to foci located in vicinity of the ampulla Newby (1958) mentioned occasional destruction of some nerve fibers in the vestibulum Shambaugh (1960) saw the same when the lumen of a semicircular canal was reached

As is the case with the facial nerve and its canal even intimate contact with otosclerosis left the vestibular nervous apparatus indifferent a fact hard to bring into harmony with the assumption of any noxious material secreted, *often during decades*, by the otosclerotic mass surrounding the nerves

The osseous *semicircular canals* are quoted as one of the predilectional sites of otosclerotic transformation. Several examples showed penetration of the endosteal layer here the mechanism was the same as described for

the innermost layer of the bony cochlear wall But even complete encircling did not result in compression of the membranous canal.

In no case did otosclerotic lesion reach the *vestibular* aqueduct.

Assault against the *cochlea* comes from the center and from the peri phery the former leads directly into the modiolus and proceeds from the direction of the cribriform plate or from the interscalar septa. Fowler (1919) illustrated extension into the septum between *basal and middle* turn. Altmann (1962) thought that ingrowth of otosclerosis into the septa, particularly between basal and middle turn, interferes with the vascular supply of the cochlea. Instances with invasion of the modiolus through the cribriform plate were rare Where the interscalar septa have been invaded the modiolus was hardly reached All in all direct damage to the nervous apparatus in the modiolar canal, e.g., compression, plays a minor role—in sharp contrast to exposure of the nerve in the internal meatus

Contact f the otosclerotic focus with the external wall of the cochlear turns is a cardinal point for potential damage through influence exerted on the anchoring syst m of the basilar membrane Goodhill (1961) em phasized that massive intracochlear lesions interfere with proper basilar membrane dynamics.

Th boundary between original and metaplastic bone was always sharp s found by Nager and Meyer (1932) by polarized light (standard in the present investigations) they stated that transitions between old and oto-sclerotic bone do not exist.

As practically every otosclerotic focus contains distinctly separated spon gious and sclerotic portions, it seemed to be of interest to see whether one or the other component i the first to reach the capsular wall Tabulations long this line failed to show predominance of one or the other Sham baugh s (1960) laminagrams showed, in half of the patients, with the possibility of cochlear otosclerosis, a spongy or partly recalcified focus. We concur with the thesis of W lff (1964) it is impossible t regard the different types of ti sue in which otosclerosis presents itself as successive stages in the dev lopment of the disease

The atla of M nasse (1917) illustrates the focus reaching the lumen of the ochlea or vestibulum after traversing the capsule (Fig 52) His descrip-tion f the proces f llows On the external wall of the spiral ligament one observes thick, globular connective ti ue prominences they can protrude far int the lumen f the cochlear duct Hydropic degeneration of the spiral ligament i never lacking the coarse band f connective tissue lining the e tcular wall f the cochlear turn is interrupted by many vacuoles, partly rhombic partly triangular mpty or filled with finely granulated masses r mucus. I netrati n of th endosteum by the advancing otosclerotic ma s wa clearly hown by his atl l (Fig. 10) of the atlas) who, however repre-sented the inner urface of the endosteum as being smooth, not deformed. Lange (1926) on the other hand saw the endosteum, wherever it was reached by the focus, more or less thickened. Shambaugh (1960) observed

the same when the lumen of a semicircular canal was reached Schuknecht, McGee, Igarashi, Fujita, and Davison (1964) saw adjacent to the advancing otosclerotic lesion, atrophy of the spiral ligament Rüedi (1964) gave several illustrations of the otosclerotic focus contacting the spiral ligament.

According to Werner (1931) the endosteal layer is lacking at the cochlear tip It is questionable whether this circumstance facilitates otosclerotic penetration in this area. Lawrence (1956) considered the extant information regarding the elements around the spiral ligament as insufficient. In agreement we found data regarding the elements around the spiral ligament inadequate and regarding the anchoring of the spiral ligament to the bone conspicuously scarce

Regarding the *anchoring of the spiral ligament* to the osseous wall of the cochlear capsule, it is not easy to gain a clear picture Neubert (1950) complained about the lack of information on the manner of the axial anchoring and about lack of data on the connection between the spiral ligament and the bony wall This wall carries (Richany Anson and Bast, 1960) through the proximal half of the basal turn a smaller secondary plate namely the lamina spiralis secundaria, opposite the osseous spiral lamina, which becomes gradually lower and finally disappears It is possible that this spine forms the basis of the otosclerotic exostoses (called sometimes enostoses) protruding almost exclusively—and, even so, rather infrequently—into the cochlear scala of the basal turn Held (1926) emphasized the importance of conditions in this region and explained how tension of the basilar membrane depends on its anchoring in the spiral ligament

Yet information on anchoring of the spiral ligament to the osseous capsule is decisive Changes made by the advancing otosclerotic mass result in deformation loosening of the basilar membrane with subtle deformation in the architecture of the Corti papilla albeit hitherto not verified under the microscope

Held (1926) gave the following description Among the cells of the walls of the two perilymphatic scales only the connective tissue cells of the spiral ligament show conspicuous histologic particularities, occupying the inner part from the insertion of the basilar membrane by a tightly stretched network of fibers The external part broadening continuously is compact and shows all endosteal characteristics of a connective tissue mass in its transition into the bony cochlear capsule itself In the inner part of the spiral ligament, connective tissue cells rich in plasma form smaller and larger nests, finely granulated and intimately connected to the walls of the vessels In the inner part of the spiral ligament another arrangement gains importance namely the insertion of the basilar membrane The fibers of the spiral ligament are at the prominent inner ledge still densely compressed here its radiating fibers dissolve into a tightly stretched reticulum with very wide meshes, in which the radial fibers are held together everywhere by transverse and oblique connecting fibers

Breschet (1836) found a gelatinous substance inserted between the bony

wall and the ba ilar membrane Henle (1866) was unable to separate the periosteum from the bone without loosening fragments from the most superficial bony lamellae Schwalbe (188) found the much thickened external wall of the cochlear duct solidly connected with the periosteum. Neubert was able to loosen the periosteum from the bone on the one side and from the external surface of the spiral ligament without difficulty According to his description the lamina spiralis secundaria, serving as attachment of the spiral ligament to the bony cochlear wall, is composed of a system of richly branched bony spines and plates.

v Békésy (1960) experienced the greatest difficulty in opening a cochlear canal as its lining of a tough, thin membrane adhered only loosely to the bone

Neubert summarized the mechanism of the peripheral anchoring in the following way The attachment of the basilar membrane is secured by the connective tissue wedge of the spiral ligament, which is divided, according t the structure of its cellular fibrous material, into three zones not sharply delimited against each other The inner portion, jutting out wedge-like contains a filling mass the fanlike deploying basilar fibers. In the median layer interwoven and anastomosing fibers create a honeycomb network with meshes, which become richer in fluid the more they approximate the t p f the cochlea. The third border layer follows outward, as a comparatively narrow dense plate rich in cells, its network forming a vertical l ttice The adjacent periosteum is distinctly thicker in the extent of the piral ligament Its fiber bundles meet in acute angles, crossing and penetrating each other and run, generally in longitudinal direction along the cochlear canal Differences in the firmness of the single constituents at the borders of the divi ions guarantee deformability f the spiral ligament

Thi deformability a shifting of the planes along each other offers ample xplanation for changes incurred by the approach of the otosclerotic mass.

According t Rüedi (1964) the spiral ligament is lower and is loosely built at th boundary to the tympanic scala, whereas the surface against the estibular scala is covered by an end thel-like layer

Turning to the changes f thi apparatus at tosclerotic foci, *one has to* consider that at the cochlear tip (frequently invaded by the otosclerotic fo- ci) the ndosteal layer may be lacking—Werner (1931) and Sercer (1968) decl red th n losteal layer t be perfectly avascular No vascular pathways connect th endosteal and the enchondral layer according to present knowledge A scularity might have to do with poor resistance against the ad ncing tosclerotic mass.

Siebenmann (1911) bserved a serous exudate in the *perilymphatic* pace f the cochlea at ext nsion of otosclerosis to the endosteum. *This ob*servati n might have offered the basis *for his* concept according to which metab lites l berated by the pathologic bone diffuse through the endosteum int the perilymph nd endolymph *of the cochlea, with damage to the* cochlear nerve endings. Going one step farther *he* assumed a serous *labr*

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Breschet (1836) found a gelatinous substance inserted between the bony

of the fibrils each fiber is transformed into a rosary-like structure. Possibly this process is repeated whenever the focus penetrates the endosteal bone and produces the fragmentation into a rosary like formation, as described in detail in Section 3. This fragmentation represents the correlate in the dimensions of the light microscope. The description of Chevance is valid to the otosclerotic focus in any location, and so it is remarkable that this enlarged form should be adopted only when contact with cochlear space is achieved. If so this phenomenon represents the most remarkable single observation hitherto formulated on the process of penetration.

Hollemann and Harril (1967) found otosclerotic involvement of the endosteal layer with regressive changes in stria and spiral ligament, such as atrophy fibrosis, hyalinization however abnormal vascular shunts were not a significant feature

Siebenmann (1911) observed that often merely a very thin septum divides the perilymphatic spaces of the cochlea from the large lymphatic spaces within the spongiosed bone. Examples of this arrangement were given in Section 3. On the other hand, atrophy of osseous tissue, of the vascular stria, of cells and nerves in the cochlea, as described by Mayer (1917) and Gray (1934) and confirmed by Nager and Fraser (1938) depend too much on the hazards of histological processing to be built definitively into the microscopic picture of labyrinthine deafness. According to this concept, a cochlea assaulted by otosclerosis would offer a picture of total demolition this obviously is not the case.

Lawrence (1966) declared the arcade vessels beneath the basilar membrane to be the nutrient vessels of the organ of Corti. According to this concept it is not the stria system which feeds the hair cells, and therefore stria-damage by the focus, approaching through the capsular wall, would not cause sensori-neural deafness. On the other hand, warping of the arcade vessels themselves might endanger the function of the organ of Corti.

In the entire process of otosclerotic penetration of the cochlea, it remains noteworthy that the contours of the intracochlear space are so widely preserved Frequently only some flattening of the concave bony contour is seen, and definite penetration by exostotic protuberances is restricted largely to the basal turn. The penetrating power peters out somehow seemingly there has to be capsular bone present to be transformed, and without this nourishment, otosclerosis loses its momentum. This might well be what Brunner called atrophy f the advancing edge a phenomenon we did not ucceed in identifying.

The inner meatus frequently is a veritable showplace of otosclerotic proliferation resulting in coarse alterations of the lumen. Concentric narrowing or excrescences into the lumen impinge on the nerve Here lies possibly the core of the problem of cochlear deafness. Manasse (1917) considered constriction of the lumen of the inner meatus by otosclerotic bone a serious influence on the function of the 8th nerve The normally smooth wall of the

rinthitis, due to metabolites passing from the otosclerotic focus into the internal ear Lindsay (quoted by Carhart 1963) similarly assumed early labyrinthitis as basis for invasion of the tympanic scala One might recall that not merely was the existence of some special secretory product of the otosclerotic mass postulated, but its origin itself has been attributed to endocrine abnormalities (Escat quoted by Klotz, 1950)

Attention has been frequently directed to the role of the *vascular stria* It is to be remembered that Fischer (1925) saw many variations in its normal histological picture frequently it is hard to decide whether one deals with normal conditions or pathologic changes

Changes in the stria vascularis caused by the approaching focus, as a possible source of lesions in the organ of Corti were mentioned by Ruttin (quoted by Siebenmann 1911) Mayer (1917) Lange (1926) Wolff (1950) Rüedi (1964)

Manasse (1912) saw at the lower end of the stria thick, round, fibrous prominences of dubious vascular origin occasionally jutting far into the lumen of the cochlear duct Mayer (1917) reported engorgement venous stasis in the vascular stria and thought it responsible for functional damage Rüedi (1964) observed circumscript increase in the vascular loops and proliferation of the epithelium of the stria while Benitez and Schuknecht (1962) showed (Fig 3) otosclerosis extending to the endosteum and creating atrophy of the spiral ligament Schuknecht Igarashi, Fujita and Davison (1964) saw atrophy of the spiral ligament with connective tissue thickening adjacent to otosclerotic lesions.

Penetration of the endosteum is the last step *before* the otosclerotic focus reaches the immediate neighborhood of the cochlear spaces. Lange (1926) saw the endosteum more or less thickened where it was reached by the focus Shambaugh (1950) noted formation of a thin layer of amorphous collagenous material beneath the adjacent connective tissue after otosclerosis had absorbed the endosteal layer of the bony capsule Manasse (1912) explained how the walls of the cochlear duct undergo hydropic degeneration *at the spiral ligament the coarse connective band lining the concavity* of the capsule becomes permeated by many partly rhombic spaces, which are either empty or show finely pulverized or mucous content

The final step penetration of the otosclerotic focus itself through the endosteal bone and the periosteum, was clearly illustrated by Manasse (1917) in his atlas (see above) This picture is remarkably similar to the numerous cases where the *focus, in its so-called predilectional* location "hesitates (to apply the appropriate expression of Hough, 1964) to step across the annular ligament

The otosclerotic *tissue itself may go through* a retrograde step when approaching the cochlear space According to Brunner (1952) the otosclerotic bone approaching the endosteum frequently becomes atrophic Chevance *(1962) saw under the electron microscope at the stag* of formation of the focus, disappearance of the collagenous tissue by a process of fragmentation

the delicate elements of the organ of Corti. Immediately under the periosteum there is frequently only a thin septum separating large lymphatic spaces from the otosclerotic area. When this septum breaks, labyrinthine pressure and position changes appear. Ruptures initiating sudden changes may explain hearing losses. Corti cells, stria vascularis, nerves, windows remain intact. Vertigo appearing with the hearing loss can be of the same origin. Menière attacks, mild or apoplectiform, could be sufficiently explained by this mechanism, offering a monistic interpretation for cochlear and vestibular damage.

In the three quarters of a century since the promulgation of this concept, there have been endless deliberations. Frequently new "theories" are presented, omitting sometimes to mention the initiator. Clash of opinions was sharp throughout this long period. Guild (1944) championed the opposition: "Atrophy of cochlear nerve fibers or of the organ of Corti does not occur more often in ears with otosclerotic areas than in ears free of otosclerosis." He was unable (as quoted by Ash and Raum, 1956) to accept any influence of otosclerosis on the cochlear apparatus. A similar stand was taken by Glorig and Gallo (1962) who found that otosclerosis does not increase sensori-neural hearing loss above that to be expected in the general population. Runge (1926) explained that combination of the effect of stapedial ankylosis and inner ear deafness may be observed with a relatively innocuous neuro-epithelial degeneration. Shambaugh (1959) observed that labyrinthine otosclerosis with cochlear loss of otosclerotic origin without stapes fixation is probably more common than generally thought; he later (1966) progressed to the opinion that stapedial and cochlear invasion are equally frequent. Rollin (1910) albeit assuming hydrops with the focus reaching the endosteum, found that Corti and vestibular end organs are left undamaged. Carhart (1962) mentioned that some of the progressive hearing losses now classified as sensori-neural deficits are probably the result of labyrinthine otosclerosis without accompanying stapes ankylosis.

In the near past, attempts toward an approach by chemical analysis appeared, not practicable in the time of Siebenmann. Wullstein, Kley, Rauch, and Koestlin (1960) wanted to objectivate toxic damage by analysis of the perilymph of operated otosclerotics. Sodium and potassium turned out to be unchanged; alkali phosphatase was increased. Besides the bone process, vascular activity within the focus was considered as potentially responsible. Rüedi (1962) saw for the theory of Siebenmann a new explanation in the investigations of Naftalin and Harrison (survey 1966) on active circulation of the labyrinthine fluids. Maurer (1962) found in different regions of otosclerotic bone decreased mineralization. He concluded (1967) that decrease in mineral content and increase in nitrogen content and in activity of alkaline phosphatase point to a higher than normal participation of fibril content in the web-like bone. Rüedi, Sanz and Fisch (1964) confirmed, in perilymph withdrawn in the course of stapedectomies, the presence of alkali phosphatase with decrease of calcium and increase of

inner meatus becomes frayed, torn up over the otosclerotic product the dura is engorged, producing a Schwartze sign" in the inner meatus Circular stenosis appeared in our material infrequently but often flat or spiny even clawlike protrusions reached deep against the nerve The possibly far reaching functional damage is hard to judge

The fundus of the inner acoustic meatus is surrounded by several layers of periosteal lamellae the enchondral layer follows the contour of the periosteal sheath while an endosteum—continuation here of the dural lining of the meatus—is hardly discernible It is possible that the lack of it is responsible for the exuberant proliferation of otosclerotic excrescences in this location

Psammomas in the inner meatus are most numerous along the frayed edges of the protruding focus and less numerous along the smoother parts of the dural lining Predominantly they aggregate along lesions of spongious, vascular nature Without suggesting any causal connection between otosclerosis and proliferation of psammomas, one might recall a number of "monistic theories according to which vascular etiology underlies all inner ear changes in otosclerosis Ever present hyperemia in these cases with invasion by the focus, might offer richer material to create similar formations of vascular origin In the inner meatus, in his case rebuilt by Paget s disease Tamari (1942) found innumerable psammomas in the sheath of the nerve Increased irritation by the formerly smooth now ragged surface may enhance their development

Influence exerted by the otosclerotic mass through secreted products was most peremptorily formulated by Manasse (1912) who declared that atrophy in the wake of otosclerosis is a regular consequence *independent of the extent or locali ation of the osseous lesion* Cray (1917 1932) echoed this conception postulating degeneration of the cochlear nerve independent of the fixation of the stapes or of any osseous change in the capsule of the labyrinth deafness occurred *before* the stapes is fixed due to primary damage to the cochlear nerve This idea claims a single developmental source for stapedial *and* cochlear deafness, caused by purely mechanical obstruction *and* metabolic damage Moritz (1955) accepted vegetative origin for half of the cases where otosclerosis was accompanied by inner ear deafness.

Siebenmann s initial concept (1899) was somewhat less transigent the focus has to reach a certain degree of change before a toxic substance is produced in sufficient concentration to cause functional damage According to his teaching the course of events can be reconstructed in the following way when the focus reaches the endosteum a serous transudate occurs within the perilymphatic cochlear spaces The metaplastic bone liberates metabolites which by way of the transudate reach the peri and endolymph spaces of the cochlea with damage to the nervous apparatus. To the changes in pressure and density of the labyrinthine fluid caused by advance of the focus, chemical alterations are added that end in nutritive damage to

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potassium and protein correlation of potassium and protein increase with preoperative bone conduction impairment could be demonstrated.

Sulfhydryl groups were claimed as indication (Chevance 1964) of respectively *destructive or constructive phases within the pathologic bone*

Schindler and Schnierer (1966) did not find any statistically verifiable difference between perilymph from otosclerotics and perilymph from patients with tympanosclerosis, congenital stapes ankylosis, Menière etc *Concentrations of sodium potassium and lactic acid dehydrogenase in perilymph* of otosclerotics have been found by Silverstein and Schuknecht (1966) to be similar to serum levels

These few examples are evidence that the need is felt to create a solid basis for the persistently quoted concept of Siebenmann Chevance (1962) expressed the hope that clarification can be expected in the not-too-distant future Existence of substances released into the labyrinthine fluids, as cause of sensori neural loss in otosclerosis, was accepted as a working hypothesis by Altmann Kornfeld and Shea (1966) But in the words of Lawrence (1966) much more information is needed on the dynamics of the normal membranous labyrinth before it can be said that a sensori neural *hearing loss can be produced by biochemical changes resulting from* otosclerosis he declared that it is not known whether chemicals toxic to the organ of Corti might be exuded by an otosclerotic focus Charachon (1967) reported on the explosion like multiplication of studies in chemistry of the labyrinth fluids in the last decade

Watson and *Tolan (1949) postulated postmortem examination to be the* only proof that a nerve deafness is indicative of otosclerosis. Brunner (1952) wanted microscopic studies continued as the final solution the problem will be solved by pathology and not from surgery Mueller (1959) declared that only morphologically verified changes in the membranous labyrinth *can decide as to the causes of inner ear damage in otosclerosis*. Bosatra (1960) acknowledged histopathology as the only absolute demonstration of stapedial ankylosis in one ear and cochlear involvement in the other Shambaugh (1960) offered clinical signs for suspecting cochlear loss without stapes fixation he emphasized, however that there is no reliable *method other* than histophathology or at least X ray to diagnose the condition Altmann (1962) considered the discrepancy between neurosensory hearing loss, and lack of histological evidence to support a similar change as disturbing Carhart *(1963) found that otosclerotic temporal bone speci*mens explaining untraditional audiological findings were still in limited supply According to Derlacki and Valvassori (1965) the 'typical picture of labyrinthine otosclerosis has not been the object of intensive study as yet the histological impasse may take years to resolve in final analysis *otosclerosis* as a clinical entity must find its decisive evaluation in the histopathologic documentation.

Contemplation of the critical area where original and metaplastic bone meet raises the *question whether a sector exists* as mentioned above between

the two, a no-man's-land carrying signs of approaching destruction. Pre-otosclerotic changes as described by Brunner are characterized by overproduction of precollagenous substance and primitive bone. In the present material, capsular and otosclerotic bone met with a very sharp boundary. This sharp outline was seen by Chevance (1962) even at a magnification of 60,000 under the electron microscope. Fingerlike protrusions are the usual form of propagation of otosclerosis, but the boundary around these is not less sharp. A still normal lamella immediately adjacent to an otosclerotic protrusion does not show any difference from the normal lamella next to it.

The otosclerotic protrusions seem to hit the lamellae generally "*head on*". This behavior contrasts with the propagation, e.g. of a carcinoma, with its tumor mass penetrating *along* the lamellae and prying them apart. It remains to be seen whether the above manner of attack can be established as characteristic of otosclerosis.

Rüus (1961) found that enchondral and endosteal layers are composed of devitalized, even necrotic bone: this fact does not deter otosclerosis from penetrating both.

As a technical remark it should be mentioned that, regarding elements of the inner ear, many reports on "atrophy" can justly be disregarded. The difficulty of obtaining adequate material with added vicissitudes of more or less success in fixation of the specimens for studies on otosclerosis was well known until the change created by the institution of the Bone Banks. Contradictions arose easily. Jones (1941) included labyrinth "atrophy" in the "typical" picture of otosclerosis, while Bosatra and others considered the "classical" picture as one where the inner ear lesion appears only in the latest stages. The present material shows that a similar time sequence cannot be asserted, as the initial assault can well be directed against the cochlear capsule.

After description of "pseudo-otosclerosis" by Moritz (1935) serious warning appeared concerning simultaneous observations of otosclerosis and inflammatory conditions, with interpretation of serous or other secretions as metabolites liberated by the otosclerotic process (s.e.g. Dietzel 1958). The difficulty of keeping apart otosclerosis and isolated stapedial ankylosis caused by adhesive processes had already been pointed out by Runge (1928). Goodhill (1960) extensively discussed the "wide range of clinical states which may mimic otosclerosis". Sooy (1960) suggested measures of management of middle ear lesions simulating otosclerosis. Today "pseudo-otosclerosis" can boast an extended literature. Nicougar (1965) systematized false otosclerosis. Schuknecht and Gross (1966) warned against identifying sensori-neural hearing loss invariably with otosclerosis, as other conditions may concur.

The first page of this presentation quoted Krepuska and Krepuska (1936) who declared it impossible to separate labyrinthine deafness, as an otosclerotic damage to the cochlear capsule, from other hearing loss of inner-ear origin.

The difficulty of diagnosing cochlear otosclerosis during life was re-emphasized lately by Shambaugh (1966) who tabulated the situations in which it should be suspected

Polytome laminagraphy with its rapid progress, may offer a valuable correlate to histologic investigation

6 SUMMARY

In 1899 Siebenmann formulated his theory according to which "meta bolites," produced by the otosclerotic bone, exercise toxic influence ending in hearing damage His theory has been adopted by numerous authors down to the very present. No evidence has turned up, under the light microscope to substantiate this concept. Results of the few chemical investigations searching after the special otosclerotic product possibly remain the only ones to deliver arguments in its favor

Our own material permitted us to tabulate cases with the otosclerotic focus in contact with the osseous cochlear capsule Statistical evaluation is futile because of the steady arrival of additional material Similar findings of other investigators give the impression they may form half of the cases especially in higher age groups.

In older patients, years after their surgery not a single instance of the so-called "burned out" focus was observed. It seemed that involvement around the cochlear capsule proceeded to reach in higher ages maximum expansion Surgical intervention, executed around the stapes did not influence further growth of the focus. The most extended transformation of all parts of the otic capsule was seen in a 77 year-old woman with hearing difficulty since age 18 and total deafness since her 2 th year

Careful observation of the capsular bone adjacent to the advancing focus did not show any structural change in the sense of a "pre-otosclerosis" Nothing poke for a softening up of the immediate surrounding in front of the advancing focus. This would be obviously one of the effects of metabolites produced by the focus Breaking through the walls—osseous and fibrous—of the capsule cochlea and vestibular was accomplished by sheer physical force pressure making the a sumption of any other form of violence unnecessary and unwarranted.

No ign of tosclerotic involvement outside the otic capsule as in the large os icles have been encountered. No preponderance of otosclerotic involvement of the fissular region was observed. A modification of the area to be called predilectional site has been suggested by Kelemen and Linthicum in 1965 The so-called congenital fissures of the temporal bone encountered frequently described by others a predilectional locations, did not show any connection with the tosclerotic process.

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Every otosclerotic focus contained spongiotic and sclerotic portions; the two components were within the focus, generally as sharply divided as was the entire focus from the original bone. Neither of the two can be assigned any preferential role in progression as to age or as to expansion. The terms "young" and "old" foci ask for serious revision, together with the traditionally assumed developmental sequence of the otosclerotic focus.

Comparison of the ante mortem bone thresholds with the histopathologic findings has shown, in this material, that the majority of individuals with otosclerotic involvement of the cochlear endosteal layer have an elevated bone conduction threshold. Contrarily only few individuals in whom otosclerosis remained restricted to the footplate or the vestibulum had a significant increase of the threshold. No correlation between the configuration of the audiogram and the portion of the cochlea involved by otosclerosis was found. However increase in the bone conduction threshold was observed in the ears, in which the basal turn, and one or more of the other turns, or the inner meatus was involved by otosclerosis.

ZUSAMMENFASSUNG

Siebenmann's Theorie laut welcher otosklerotischer Knochen Stoffwechselprodukte erzeugt, die durch Giftwirkung Hörschaden erzeugen, war 1899 formuliert und fand zahlreiche Anhänger. Unter dem Lichtmikroskop waren keine Beweise aufgetaucht, um diese Theorie zu unterstützen. Ergebnisse chemischer Untersuchungen die nach dem spezifischen otosklerotischen Produkt fahnden, könnten möglicherweise in bejahendem Sinne ausgelegt werden.

Berührung zwischen Schneckenkapsel und otosklerotischem Herd war in unserem Materiale in Übereinstimmung mit Befunden, oder wenigstens Vermutungen, anderer Autoren, so häufig gesehen, dass es sich dabei um die grössere Hälfte der Fälle handelte. Dies gilt vor allem für ältere Altersgruppen. Tabulierung wurde unterlassen, da Einlaufen von weiterem Material häufige Änderungen erfordert.

Auch in ältesten Patienten kam kein einziges Beispiel von einem sogenannten „ausgebrannten" Herd zur Beobachtung. Es scheint, dass Einbeziehung der Schnecken- und Vorhofkapsel in höherem Alter weiteste Ausbreitung erreicht, sowohl das spongiöse wie das sklerotische Element betreffend. Peristapediale Eingriffe haben das Weiterwachsen des Herdes nicht beeinflusst. Weiteste Einbeziehung aller Teile der Schneckenkapsel war in einer 77 Jahre alten Frau beobachtet; sie war seit ihrem 18. Jahre schwerhörig und seit ihrem 27. Jahre vollständig taub.

Die Knochenpartie der Innenohrkapsel, angrenzend an den vordringenden Herd bot keine strukturelle Änderungen dar im Sinne einer sogenannten pre-Otosklerose. Nichts zeugte z. B. von einer Auflockerung gegenüber dem fortschreitenden Herd, ähnlich als man dies als ein Effekt der von dem Herd angeblich erzeugten Giftstoffe fordern müsste. Durchbruch von Wandungen, in Schnecke und Vorhof, wird durch eine einzige *physische* Kraft vollbracht, nämlich Druck. Annahme einer jeden sonstigen Einwirkung erübrigt sich.

Ausserhalb der Innenohrkapsel war keine Spur einer otosklerotischen Umwandlung zu bemerken, so auch nie in den Gehörknöchelchen. Änderung der Bezeichnung „bevorzugter Sitz" „Prädilektionsstelle" des Herdes war 1965 von Schuknecht und Lindsay vorgeschlagen. Sogenannte kongenitale Spalten des Schläfenbeines waren häufig beobachtet ohne Anhaltspunkte sie mit Otosklerose in Bezug zu bringen. Ebensowenig war dies der Fall für die Gewebe die in die fissulare Gruppierung einbegriffen sind.

Jeder otosklerotische Herd enthielt spongiöse *und* sklerotische Anteile. Die beiden waren, innerhalb des Herdes so scharf gegeneinander abgegrenzt,

Comparison of the ante mortem bone thresholds with the histopathologic findings has shown in this material that the majority of individuals with otosclerotic involvement of the cochlear endosteal layer have an elevated bone conduction threshold Contrarily only few individuals in whom otosclerosis remained restricted to the footplate or the vestibulum had a significant increase of the threshold No correlation between the configuration of the audiogram and the portion of the cochlea involved by otosclerosis was found However increase in the bone conduction threshold was observed in the ears, in which the basal turn and one or more of the other turns, or the inner meatus was involved by otosclerosis.

RÉSUMÉ

Depuis 1899 quand Siebenmann a formulé sa théorie selon laquelle les métabolites qui sont produits par l'os otosclérotique, et qui exercent une influence toxique resultant en degât de l ouie elle a été adopté par un grand nombre d'auteurs. Aucune evidence microscopique a été découverte pourtant pour confirmer cette hypothèse Les résultats des rares investigations chimiques dans lesquels le produit spécial otosclérotique a été cher ché sont peut être les seules confirmant cette théorie.

Nous pouvons baser une tabulation des cas avec un foyer otosclérotique en contact avec la capsule osseuse cochléaire sur nos matériaux cliniques. Une évaluation statistique serait futile a cause de la constante présentation de matériel supplémentaire Les trouvailles similaire d autre investigateurs donnent l'impression qu ils peuvent former la moitié des cas, particulièrement dans les groupes d'âge les plus avancés.

Parmi les malades les plus âgés, pas une seule instance de soi-disant burned out foyer a été observé, même plusieurs années depuis leur chi rurgie On dirait que l envahissement autour de la capsule cochléaire a procédé d atteindre une expansion maximum dans les âges avancés. L'inter vention chirurgicale dans le voisinage de l étrier n a pas influencé la croissance subséquente du foyer La transformation la plus étendue de tous les parties de la capsule otique a été évident chez une vieille femme de 77 ans qui avait eu une difficulté auditoire depuis l age de 18 ans, et une sourdité complète depuis l'âge de 27 ans.

Une examination minutieuse de la capsule osseuse adjoint au foyer progressif n a pas demonstré aucune altération de structure dans le sens d'une pré-otosclérose Rien n'indique une ramollissement du tis ue a l entou rage ou devant le foyer progres if Ceci serait sans doute une des effets des métabolites produit par le foyer Le creusement à travers les murs, osseuse t fibreuses, cochléaire et vestibulaire de la capsule a été accompli par force physique avec pres ion. Par uite ce n était ni nécessaire ni justifiable d accuser aucune autre force

Aucun indication d'exten ion du processus otosclérotique hors de la cap ule otique comme dan les grand ossicles, a été rencontré Aucune enva hisseme t otosclérotiq de la région fissulaire a été bservé Une modification d l'end it qui devait être appelé l site de predilection a été suggéré par helemen et Linthicum en 1965 Les soi-disant fissures congénitales de l os temporal, qui sont rencontrés souvent, et qui ont été décrites par des utres comme it d prédilection, n nt pas démontré aucune relation avec le proces u tosclérotique

wie der vollständige Herd gegen den umgebenden ursprünglichen Knochen Keine der beiden Komponenten konnte eine Vorzugsrolle beanspruchen, weder bezüglich Alter noch Art des Fortschreitens. Bezeichnungen wie „junge" respektive „alte" Herde fordern ernsthafte Revision gleichzeitig mit der ganzen, traditionell festgelegten Sequenz des metaplastischen Prozesses

Vergleichung der ante mortem Knochenleitungsschwellen mit den histopathologischen Befunden zeigte in diesem Material, in der Mehrzahl der Individuen mit otosklerotischer Einbeziehung des kochlearen Endosteum eine Erhöhung dieser Schwelle Dagegen zeigten nur wenige Individuen in denen die Otosklerose auf die Fussplatte oder den Vorhof beschränkt blieb, eine erhebliche Erhöhung der Knochenleitungsschwelle Zwischen der Konfiguration des Audiogramms und der durch Otosklerose ergriffenen Partie der Schnecke bestand keine Korrelation Doch war Erhohung der Knochenleitungsschwelle in den Ohren zu vermerken in denen die basale Windung und eine oder mehrere der übrigen Windungen, oder der innere Gehorgang in den otosklerotischen Prozess einbezogen waren.

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Depuis 1899 quand Siebenmann a formulé sa théorie selon laquelle les métabolites qui sont produits par l'os otoscléroticque, et qui exercent une influence toxique resultant en degât de l'ouïe, elle a été adopté par un grand nombre d'auteurs. Aucune évidence microscopique a été découverte pourtant pour confirmer cette hypothèse. Les résultats des rares investigations chimiques dans lesquels le produit spécial otosclérotique a été cherché sont peut être les seules confirmant cette théorie.

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Tout foyer otosclérotique consiste de portions spongieux et sclérotique les deux parties constituantes était généralement nettement divisé dans le foyer comme le foyer entier était de l os original ni l un ni l autre ayant droit d un rôle préférentiel dans le processus a cause d âge ou d expansion On peut demander une revision sérieuse de termes « foyer jeune » et « foyer âgé » et de développement supposé traditionellement, du foyer otosclérotique

Une corrélation du seuil de la conduction osseuse *ante mortem* avec les trouvailles histopathologiques obtenu dans ces matériaux indique que la plupart des cas avec envahissement otosclérotique de l endosteum de la cochléa avait un élévation du seuil de la conduction osseuse Par contre chez peu de cas ou l otosclérose était limité à la base de l étrier ou au vestibule, on a observé une élévation significante du seuil de la conduction osseuse Il n avait aucune relation entre la configuration de l audiogram et les parties de la cochléa envahi par l otosclérose On a trouvé que le seuil de la conduction osseuse avait la tendance d être élevé dans ces oreilles dont la courbe basale et une ou plus d autre courbes, ou le canal auditoire interne étaient envahi par le processus otosclérotique

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EDITOR TOKURO SUZUKI

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INTRODUCTION

T SUZUKI

From the Department of Otolaryngology Faculty of Medicine, Shinshu University Matsumoto, Japan

The auditory responses in experimental animals were recorded from electrodes placed directly in or on the cochlea, acoustic nerve, central auditory pathway or sensory cortex. Such direct inserting of electrodes can not be administered in man. By indirect leads, however the responses evoked by auditory stimuli are markedly attenuated by surrounding tissue, and the signals are difficult to separate from ambient noises.

This insuperable barrier of recording human evoked responses has been surmounted by the recent development of electronic computers. The averaging technique by using a computer has made it possible to identify small evoked responses which are otherwise masked with electrical background activity The averaging technique was applied initially to the recording of the cortical evoked responses to sensory stimuli by Dawson (1954), Rémond (1956), Barlow (1957) and Geisler et al. (1958). In 1960 Lowell and associates first reported the application of a special purpose analog computer to the detection of the evoked cortical response to auditory stimulation, and in the next year they measured auditory thresholds of 54 normal adults by applying the averaged evoked response to auditory stimulus as an index of hearing. The computer used in their measurements, however integrated only the three or five gates of 2 msec width set at 20 to 50 msec after the stimulus. Consequently they did not record slow cortical evoked responses with latency of more than 50 msec.

Since the descriptions of Williams and Graham (1963) and Davis and Yoshie (1963), attention was focused on the application of the "slow" cortical evoked response, or vertex potential" to auditory stimulus for evaluating hearing acuity Extensive research reported since has proved that the method is a reliable and valid means of measuring hearing thresholds of infants, young children mentally retarded individuals and noncooperative adults. The method is established and called cortical audiometry (Cody and Bickford 1965), evoked response audiometry (Davis, 1968) or computer audiometry (Theissing, 1967). Recent investigations suggest that the averaged slow cortical response can be utilized not only to the determination of hearing threshold but also to the

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diagnosis of disorders at the level of the central auditory pathway (*Theissing* 1967) and the objective measurement of recruitment (Cody et al 1968).

Early components of the auditory evoked response was first described by Geisler et al. (1958). Bickford et al. (1964) claimed that these components arose from muscles of the neck and their end organ receptor was the *vestibular rather than the auditory* apparatus. On the other hand Horwitz et al (1966) and Goldstein and Rodman (1967) stated that the early components of the evoked response to acoustic stimuli is serviceable to the determination of hearing thresholds.

Kiang and associates reported in 1963 an averaged evoked response to clicks from the human postauricular area. The authors regarded the response as an auditory myogenic response. Its application to audio metric purposes has not yet been reported.

There are a number of pioneering studies on the record of more peripheric auditory responses in man The human cochlear microphonics was first recorded by Fromm et al (1935) with an electrode introduced through a drum perforation The auditory nerve action potential was measured initially by Ruben et al (1960) from the round window which *was surgically exposed. Lately non surgical recording* of *these responses* were developed by Yoshie et al (1967 1968), Portmann et al (1967 1968), Sohmer et al (1967) and Spreng and Keidel (1967). Averaging technique was utilized for recording the responses.

The purpose of the electrophysiological measurements of human auditory responses is twofold (1) objective assessment of hearing acuity for noncooperative subjects, (2) investigation of the anatomical location and nature of auditory defects by comparing data obtained from different levels of the auditory system Although a significant advance has been achieved within the last few years in the recording of the human auditory responses, difficulties still persist for obtaining useful diagnostic informations from the recorded responses. This monograph is devoted to our efforts to improve the recording technique of the *human auditory responses* and to develop the methods into useful clini cal tools for diagnosing disorders of auditory function

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EVOKED RESPONSE AUDIOMETRY IN NEWBORN INFANTS*

K. TAGUCHI, T W PICTON J A. ORPIN and W S. GOODMAN

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The auditory evoked responses of normal infants during natural sleep were recorded using an averaging computer The evoked responses had two prominent components (P and N_1), which in deep sleep were of larger amplitude and of longer peak latency than in light sleep. The infants showed lower thresholds to lower frequency stimuli. The thresholds of infants less than two days old were higher than those of older infants. The peak latency of component N_1 was longer in younger infants especially in deep sleep. There was significant air bone gap in the thresholds of infants under two days old; this indicates a conductive hearing impairment in the early days after birth. Infant maturity cannot be determined precisely through study of the evoked responses because of their great variability

The object of this study was to establish a hearing standard for normal newborn infants. This standard could then be applied to any effective newborn screening programme, and could act as a baseline in the further study of the response of the central nervous system to sound.

It has been generally agreed that there can be recorded at the vertex a long latency response to sound generated from the cortex. Usually this response is too small to be recognized in the background electrical activity of the brain. The use of the averaging computer has, however made it possible to separate this response from the ongoing electroencephalogram. Recently many researchers (Barnet and Goodwin, 1965 Engel 1967 Goodman et al. 1964; Graziani et al. 1968 McCandless and Best 1964 Price and Goldstein, 1966 Rapin 1964 1967 Suzuki and Taguchi, 1968 Weitzman et al. 1962) have established that this method enables one to evaluate the auditory thresholds of young children and infants. They also found that evoked responses during sleep were much more easily detectable than those during the waking state because of the larger amplitude of the response and the greater ease in the handling of the subject. Fortunately almost all newborn infants will sleep after being fed and therefore can be

Supported by the Medical Research Council of Canada, and the Canadian Lif Insurance Association.

tested without sedation

MATERIALS AND METHODS

Subjects

Two hundred and fifty newborn infants, six hours to twelve days old were tested for air conduction auditory responses. In another series of tests to compare air conduction and bone conduction thresholds sixty infants four hours to ten days old were studied Ten of those were retested after an interval of three days. All infants had birthweights greater than 2, 500 g

Equipment

The responses were recorded in a manner similar to that previously used in our Department by Dr Shirley Appleby (Goodman et al 1964). A block diagram of the equipment is shown in Figure 1 The electroencephalogram was continuously observed as a monitor of sleep stage by means of a Beckman Type RB Dynograph. Electroencephalographic averaging over a period of 1024 msec subsequent to the sound stimulus was done on a Fabritek 1052 Signal Averager The average evoked response was transcribed onto graph paper by a Moseley 7005 A X Y recorder

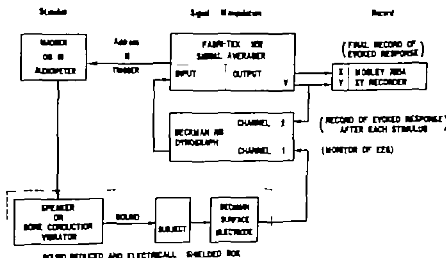


Fig. 1 Block diagram of equipment.

The sound stimulus was a short tone burst of frequencies 500 1000 or 2000 Hz from a *modified Madsen Electronics* (Model OB 60) Audiometer Its duration was 60 msec with a rise and decay time each of 30 msec. The free field stimulus was calibrated to ISO 1964 standard

using a Brüel and Kjaer Precision Sound Level Meter Type 2203 with an oscilloscope monitor The bone conduction stimulus was calibrated to normal adult forehead threshold by repeated subjective testing Thirtytwo stimuli were presented at a rate of one every five seconds since preliminary experiments had indicated that this presentation gave the best results.

Procedure

The tests were performed after the 10 00 a. m. or 2 00 p. m. feeding period in a small room across the hall from the nursery Beckman surface electrodes were applied to the vertex near the anterior fontanel (active electrode), to the right mastoid area (reference electrode) and to the left mastoid area (grounded electrode). The sleeping baby in the usual hospital bassinet, was then placed in the specially con structed sound reduced electrically shielded box. The baby could be observed at all times through the closed glass door by a nurse

Testing was performed during light or deep sleep but not during paradoxical sleep corresponding to the REM stage of adults. Light sleep was characterized by a low voltage irregular electroencephalogram with some spindle bursts deep sleep showed high voltage slow activity with some superimposed spindling. In the air conduction study the stimulus was first presented to the newborn at 70 dB It was then decreased in intensity by 20 dB steps down to 10 dB. A stimulus of 10 dB less than the lowest intensity eliciting a response was also given. At the end of the test the stimulus was presented at 90 dB to obtain a definite res ponse to aid in the interpretation of the weaker responses. The bone conduction testing was similar except that the initial stimulus was at an intensity of 50 dB.

RESULTS

Air Conduction Testing

Among the two hundred and fifty infants tested according to the described method, excellent results were obtained in 220 infants (Table 1). No infants with birth weights less than 2,500 g were tested and

TABLE 1. *Ratio of succeeded determination of threshold to sound.*

Infants-Three thresholds were obtained	220	(88.0%)
Infants-One or two thresholds were obtained	8	(3.2%)
Infants-Showed good responses to several intensities but no threshold was obtained	11	(4.4%)
Infants-No result was obtained, because of their shortness of good sleep or their movement	11	(4.4%)
Total	250	(100.0%)

tested without sedation

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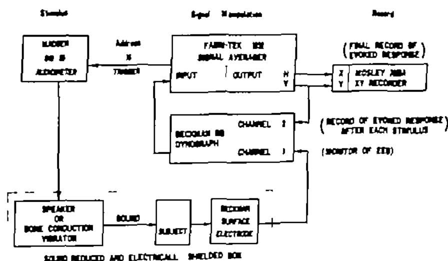
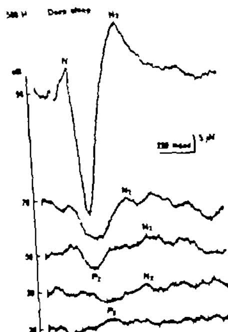


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F g. 3. Determination of threshold. Estimated threshold is 30 dB.

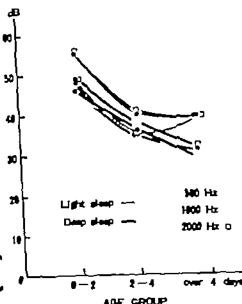


Fig. 4. Mean threshold vs. age group.

TABLE 3. *Threshold for auditory evoked response: Mean and standard deviation of thresholds (Decibels above ISO audiometric zero level).*

Age group	Number of subjects	Light sleep Stimulus frequency (Hz) 500	1000	2000	Number of subjects	Deep sleep Stimulus frequency (Hz) 500	1000	2000
0 2 days	22	49±13 (30-70)	55±11 (40-80)	50±14 (30-80)	18	46±24 (30-60)	43±12 (30-70)	40±11 (30-70)
2-4 days	35	35±13 (20-70)	40±14 (20-80)	41±15 (20-70)	24	36±16 (10-70)	35±13 (20-70)	35±14 (20-70)
Over 4 days	17	30±15 (10-70)	30±18 (20-70)	30±19 (10-70)	47	29±15 (10-70)	31±14 (10-70)	32±13 (10-70)

The figures in brackets mean the range of thresholds.

Th esholds

The threshold for evoked response audiometry was taken to be the minimal stimulus intensity which elicited a detectable cortical response (Fig. 3). The thresholds obtained listed in Table 3 and the mean threshold is plotted against age in Figure 4. The infant's threshold decreased with decreasing frequency ($P<0.01$). Infants less than two days old showed higher thresholds than those over two days old ($p<0.01$). Responses were considerably larger in deep sleep than in light

TABLE 2. *Means with standard deviations of body weight and gestational period at birth in 220 infants which showed excellent results*

Age group	Body weight at birth (g)	Gestational period at birth (days)
0-2 days	3410±438 (N=55)	279±13 (N=54)
2-4 days	3455±401 (N=74)	280±12 (N=[illegible])
Over 4 days	3358±387 (N=91)	281±14 (N=88)
Total	3402±311 (N=220)	280±17 (N=[illegible]14)

* Gestational periods of six infants were not assessed.

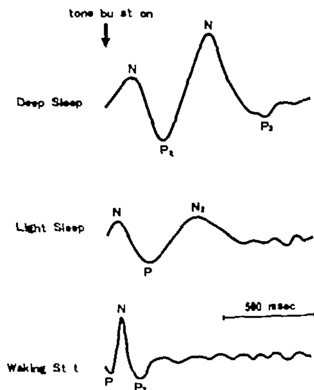
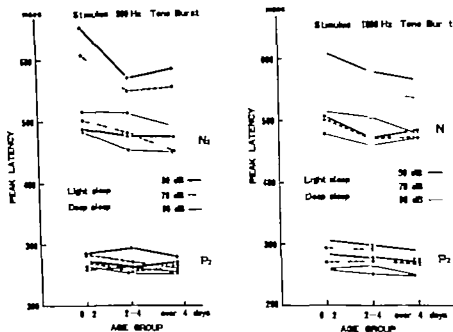


Fig 2. Changes of evoked response with stages of sleep. Upward deflection indicates negativity at vertex electrode.

the minimal gestational period of these infants was 252 days (Table 2). The evoked response of the infant had two prominent components P_2 and N_2 (Figure 2). Other components seen in adult responses (P_1 N_1 P_3) were uncommon in sleeping infants. Statistical analysis of the results was done using an analysis of variance. Since the stage of sleep changed during the testing however statistical analysis was quite difficult Measurements were compared only when obtained in the same stages of sleep this resulted in a considerable reduction in the amount of data available for analysis.



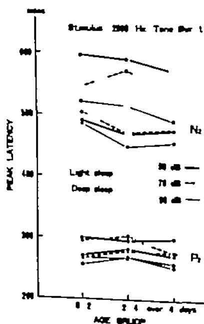


Fig. 5. Mean peak latency

TABLE 4. *Peak latency of component P_2. Mean and standard deviation (msec).*

Age group	Stimulus frequency Hz	Light sleep Stimulus intensity (dB) 50	70	90	Deep sleep Stimulus intensity (dB) 50	70	90
0-2 days	500	273±20	272±33	265±21	255±18	283±39	259±29
		(N=10)	(N=19)	(N=15)	(N=11)	(N=16)	(N=16)
	1000	284±27	270±32	253±32	305±23	293±49	258±23
		(N=10)	(N=19)	(N=15)	(N=11)	(N=16)	(N=15)
	2000	270±33	270±29	267±36	299±31	296±47	258±31
		(N=10)	(N=19)	(N=15)	(N=11)	(N=16)	(N=16)
2-3 days	500	262±35	254±31	254±21	292±33	273±38	287±35
		(N=17)	(N=22)	(N=15)	(N=17)	(N=20)	(N=17)
	1000	278±33	272±30	251±26	296±27	291±47	264±28
		(N=17)	(N=22)	(N=15)	(N=17)	(N=20)	(N=17)
	2000	281±31	279±30	266±34	295±43	303±57	268±41
		(N=17)	(N=22)	(N=15)	(N=17)	(N=20)	(N=17)
Over 4 days	500	269±13	267±31	253±29	277±28	262±30	253±16
		(N=10)	(N=15)	(N=14)	(N=42)	(N=44)	(N=38)
	1000	273±32	267±37	248±32	257±35	274±33	250±15
		(N=10)	(N=15)	(N=14)	(N=42)	(N=44)	(N=38)
	2000	272±31	277±35	258±32	299±38	275±30	253±26
		(N=10)	(N=15)	(N=14)	(N=42)	(N=44)	(N=38)

The figures in the brackets mean the number of subjects.

TABLE 5. *Peak latency of component N_2. Mean and standard deviation (msec).*

Age group	Stimulus frequency Hz	Light sleep Stimulus intensity (dB) 50	70	90	Deep sleep Stimulus intensity (dB) 50	70	90
0-2 days	500	486±58	501±69	483±48	653±57	606±67	515±36
		(N=11)	(N=15)	(N=14)	(N=11	N=15	N=15
	1000	505±52	501±53	477±55	608±53	585±59	513±50
		(N=11)	(N=15)	(N=14)	(N=11)	(N=15	N=15
	2000	489±79	502±63	488±73	595±49	544±58	520±52
		(N=11)	(N=15)	(N=14)	(N=11)	(N=15)	(N=15)
2-4 days	500	475±52	479±71	452±33	589±62	547±61	512±59
		(N=13)	(N=15)	(N=15)	(N=15)	(N=15)	(N=20)
	1000	470±48	471±69	458±35	576±48	546±60	502±41
		(N=13)	(N=15)	(N=15)	(N=15)	(N=15	(N=20)
	2000	467±67	467±56	448±34	588±54	570±75	513±51
		(N=13)	(N=15)	(N=15)	(N=15)	(N=15)	(N=20)
Over 4 days	500	473±46	450±73	449±61	531±63	552±63	490±39
		(N=10)	(N=11)	(N=12)	(N=33)	(N=39)	(N=37)
	1000	482±30	471±54	470±61	562±55	537±63	478±33
		(N=10)	(N=11)	(N=12)	(N=33)	(N=39	(N=37)
	2000	473±28	473±46	454±37	569±57	523±54	458±30
		(N=10)	(N=11)	(N=14)	(N=33)	(N=39)	(N=37)

The figures in the brackets mean the number of subjects.

TABLE 7 *Difference between air conduction threshold and bone conduction threshold in deep sleep Mean and standard deviation (dB).*

Age group	Number of subjects	Stimulus frequency (Hz) 500	1000	2000
0-2 days	20	17.0±12.0 (0—40)	22.5±13.0 (0—40)	11.0±9.8 (0—40)
2-4 days	20	5.5±6.9 (0—20)	7.0±8.0 (0—30)	3.5±8.1 (10—10)
Over 4 days	20	1.5±7.5 (10—20)	4.0±8.8 (10—30)	3.0±6.6 (10—20)

The figures in the brackets mean the range of differences between air-conduction threshold and bone-conduction threshold.

decreased very significantly with decreasing intensity ($p < 0.01$). The amplitude of the response is significantly greater in deep sleep than in light sleep ($p < 0.01$) except for infants less than two days old. The response to stimuli of 70 and 90 dB in deep sleep was of smaller amplitude in infants under two days than in those over two days (p 0.05).

Bone Conduction Testing

Bone conduction evoked response thresholds were obtained in 60 infants. The difference between air conduction and bone conduction thresholds were very significant within 2 days from birth ($p < 0.01$) and there was a tendency for such a gap to become insignificant after two days (Table 7). This finding was further corroborated by the fact that 10 infants examined within 2 days from birth showed a significant air bone gap ($p < 0.05$) but had no significant air bone gap when retestd after an interval of 3 days (Figure 6). This suggested that young infants have a conductive hearing impairment during the first few days after birth.

DISCUSSION

This present series of tests on newborn infants began with the intention of obtaining valid estimations of normal infant auditory thresholds in order to set up an auditory screening program for new born infants. The results obtained show that the infant's cortical evoked response to sound is affected by the stage of sleep the maturation of the infant and the presence of a conductive hearing impairment im mediately after birth.

Aserinsky and Kleitman (1955), Roffwang et al. (1964) and Weitzman et al. (1965) stated that the newborn infant has two stages of sleep

TABLE 6 *Amplitude ($\overline{P_2N_2}$) of evoked response Mean and standard deviation* (μV).

Age group	Stimulus Frequency Hz	Light sleep Stimulus intensity (dB) 50	70	90	Deep sleep Stimulus intensity (dB) 50	70	90
0-2 days	500	8.[illegible]±3.3 (N=13)	10.7±5.9 (N=21)	31.0±10.8 (N=13)	8.2±3.4 (N=1[illegible])	1[illegible].9±8.0 (N=18)	38.8±18.4 (N=18)
	1000	6.5±1.9 (N=13)	10.5±5.[illegible] (N=21)	28.0±13.5 (N=13)	7.[illegible]±[illegible].4 (N=12)	9.2±3.[illegible] (N=18)	28.6±1[illegible].4 (N=18)
	2000	7.6±2.8 (N=13)	9.2±3.0 (N=21)	20.3±9.7 (N=13)	6.3±2.6 (N=1[illegible])	9.6±6.1 (N=18)	27.6±15.1 (N=18)
2-4 days	500	7.9±3.5 (N=19)	10.4±3.8 (N=20)	29.6±11.6 (N=14)	10.1±3.5 (N=16)	15.4±4.4 (N=17)	46.7±16.[illegible] (N=16)
	1000	7.0±3.6 (N=19)	10.0±3.7 (N=20)	24.8±8.7 (N=14)	9.1±3.4 (N=16)	15.4±6.6 (N=17)	36.6±13.6 (N=16)
	2000	7.3±2.8 (N=19)	9.7±4.1 (N=20)	21.0±7.6 (N=14)	8.3±3.4 (N=16)	18.4±13.0 (N=17)	37.7±17.4 (N=16)
Over 4 days	500	7.9±3.9 (N=13)	10.8±4.6 (N=16)	[illegible]4.6±6.4 (N=1[illegible])	10.2±3.7 (N=43)	16.9±9.0 (N=44)	41.1±1[illegible].4 (N=39)
	1000	7.0±1.7 (N=13)	10.4±3.6 (N=16)	4.4±10.1 (N=1[illegible])	8.9±3.3 (N=43)	13.4±5.4 (N=44)	35.8±11.3 (N=39)
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The figures in the brackets mean the number of subjects.

sleep and this seemed to result in the lower thresholds obtained during deep sleep ($p<0.05$).

Peak Latencies

The peak latencies of P_2 and N_2 were measured (Tables 4 and 5 Figure 5). Negative trials, when responses were not identified were disregarded in calculating means. Waves P_1 N_1 and P_3 were so often absent that no reliable means for them could be obtained It is obvious that there was a significant difference of peak latency between light and deep sleep (P_2 $p<0.05$ N $p<0.01$). The mean peak latency of component N_2 was longer in younger infants especially during deep sleep ($p<0.01$), but there was no significant differences in the mean peak latencies of P of the three age groups ($p>0.05$). There were no differences in latency among the three frequencies (p 0.05) except for P at 70 dB ($p<0.01$). It is noteworthy that with an increase in intensity of stimulus there was a decrease in the latencies of both components P_2 and N_2 ($p<0.01$).

Amplitude

The peak to peak amplitude ($\overline{P_2N_2}$) of the evoked response was measured at the intensities of 50 70 and 90 dB (Table 6). Amplitude

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2-4 day	20	5.5±6.9 (0—20)	7 0±8.0 (0—30)	3.5±8.1 (10—10)
Over 4 day	20	1.5±7 5 (10—20)	4.0±8.8 (-10—30)	3.0±6.6 (-10—20)

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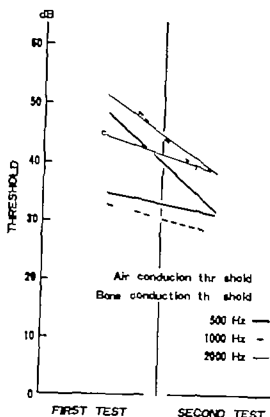


Fig. 6. Comparison of air-conduction threshold with bone conduction threshold. Means of ten subjects.

a quiescent and an active phase Quiescent sleep shows high voltage slow wave EEG activity and active sleep has a characteristic low voltage fast EEG activity In adults there are significant changes in amplitude and latency of the evoked response components during different sleep stages (Weitzman and Kremen 1965 Williams et al 1962 and 1964). In infants the changes seem to be basically the same as in adults (Suzuki and Taguchi 1968 Weitzman et al 1965). Our present results agree with these reports, except that we found no difference in P_2 peak latency between age groups. Barnet and Goodwin (1965) stated that larger amplitudes and longer latencies were often associated with deeper sleep but this effect was less in infants than in adults. Our present study showed that there was no difference in response amplitude between light and deep sleep in our youngest age group although there was a significant difference in the older infants. We think that such a finding suggests the further development of the sleep stages after birth

Infant maturational changes must be considered in this kind of testing This study showed a decrease in N_2 latency as a function of age. Barnet (1965) reported that the evoked response latency to sound (P_2) seemed to remain constant or to increase slightly for about six weeks after birth and then to decline. Engel (1967) stated that the

mean peak latency of P_2 was longer in younger infants than in older children or adults.

Our present study of bone-conduction thresholds suggests that the high air conduction thresholds obtained in younger infants are caused by an incomplete conductive mechanism. This is a new finding. The middle ear is fully formed by the last month of fetal life (Bast and Anson 1949, Eggston and Wolff 1947), but some mesenchymal tissue remains in the tympanic cavity right after birth (Igarashi, 1968) which could account for a conductive hearing impairment.

An evoked response screening test can be performed by presenting 70 dB tone bursts of 500, 1000 and 2000 Hz frequencies to an infant 2 to 4 days old during deep sleep. If the infant has normal hearing there will be an easily recognizable response to 32 stimuli presented at a rate of one every 5 seconds. We have so far successfully screened 100 infants by this procedure.

Our present overall screening programme involves several steps. The infant is initially tested for behavioural responses to warble tones by trained volunteers. If the response is questionable the infant is retested by an audiologist. If again no response is obtained the infant undergoes the evoked response screening test previously described. Questionable results on this test will entail complete evoked response audiometry and intensive further medical evaluation of the child.

Using cortical evoked responses we have established the auditory thresholds of normal infants. We believe that evoked response audiometry has a very significant part to play in any newborn auditory screening programme.

ACKNOWLEDGEMENTS

The authors are indebted to Mrs. Erika Goegginger for assistance with clinical recordings, to Mr. Earl Brown for technical assistance, and to Miss Betty Clarkson for statistical analyses.

ZUSAMMENFASSUNG

Die vorliegende Untersuchung wurde durchgeführt, um einen Masstab für die Beurteilung des normalen Neugeborenengehörs zu erhalten, der für Reihenuntersuchungen verwandt werden kann. Die auditorisch hervorgerufenen Reaktionen ("evoked responses") des sich im natürlichen Schlaf befindenden Säuglings wurden unter Benutzung eines Computers registriert. Als Stimuli wurden in einem Abstand von je 5 Sekunden Schalltöne ("tone bursts") von je 500, 1000 und 2000 Hz Frequenz angewandt. Jede Gesamtreaktion setzte sich aus 32 Einzelreaktionen zusammen. Die Reaktionen des schlafenden Kleinstkindes hatten zwei bemerkenswerte Komponenten P und N. Ungewöhnlich dagegen waren die beim Erwachsenen vorkommenden Komponenten P, N oder P. Die zwei Hauptkomponenten der hervorgerufenen Reaktionen waren in tiefem Schlaf grösser als in oberflächlichem

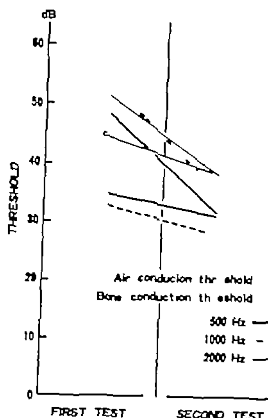


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und zeigten längere Spitzenlatenzen. Die Säuglinge hatten bei niedrigen Frequenzen einen besseren Schwellenwert. Neugeborene, die jünger als zwei Tage alt waren, zeigten im Vergleich mit älteren eine schlechtere Schwelle. Bei jüngeren Neugeborenen besonders im tiefen Schlaf war die mittlere Spitzenlatenz zur Komponente N_2 länger Ausserdem wurden in der Amplitude der Reaktionen während tiefen Schlafens signifikante Differenzen zwischen der Altersgruppe unter 2 Tagen und der über 2 Tagen gefunden. Ein signifikanter Unterschied der Luftleitungs und Knochenleitungs schwelle wurde in der Altersgruppe unter 2 Tagen festgestellt. Es ist anzunehmen dass in den ersten Tagen nach der Geburt eine konduktive Schwerhörigkeit vorliegt. Die Individualität der hervorgerufenen Reaktionen kann so variabel sein dass die Maturität des Prüflings durch obige Untersuchungen nicht präzise festgelegt werden kann.

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Acta oto-laryngologica, Supplementum 252, 19-28 (1969)

AVERAGED EVOKED RESPONSE AUDIOMETRY (ERA) IN YOUNG CHILDREN DURING SLEEP

T SUZUKI and K. ORIGUCHI

From the Department of Otolaryngology Faculty of Medicine Shinshu University Matsumoto Japan

Thresholds of averaged evoked response to uditory stimulation for sleeping young children were compared with thresholds obtained from conditioned orientation reflex (COR) audiometry Forty seven normally hearing children aged 4 months through 4 years nd 133 hard-of hearing children aged between 1 and 5 years were tested. Of these, data from 42 normal and 92 hearing impaired children were available for the comparison. The evoked response was recorded using tone bursts of 500, 1000, 2000 and 4000 Hz. They had 25 msec rise and fall time and 100 msec duration and were delivered every 5 sec. Approximately 30 responses were averaged during test run. The test was administered in sleep stages 3 and 4 of the classifi cation of Dement and Kleitman. COR audiometry was made according to the original method of Suzuki and Ogiba.

For normal children the mean difference between both thresholds was 10.38 dB, COR threshold more sensitive, and 98.2 per cent of measurements fell withi the range between 0 and 20 dB. For slightly or moderately impaired children the mean difference decreased to 6.38 dB, COR thresholds more sensitive For severely impaired subjects the mean difference was only 0 43 dB, evoked response more sensitive. Significantly smaller difference between evoked response threshold and COR threshold was proved statisti cally in hard-of hearing children than in normal children.

The literature is growing rapidly with reports on the use of aver aged evoked response to acoustic stimuli for assessing hearing acuity of young children and noncooperative adults. The term "evoked res ponse audiometry (ERA)" is now widely accepted for this technique. For validating the audiometric application of the evoked response some investigators compared the evoked response threshold with volun tary or beha ioral audiometric threshold in adults (Cody et al. 1965 Davis, 1966 McCandless et al. 1966 1968; Suzuki et al. 1965) and in children (Davis, 1965 1966 Davis et al. 1967 McCandless, 1967 Price et al 1966), most of them indicating an excellent approximation of both thresholds. However few reports have been published on the validation of ERA in young children where this technique is needed most. It is of course due mainly to the lack of reliable methods for determining accurate hearing acuity of young children.

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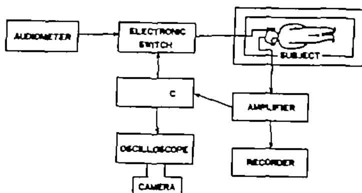


Fig 1 Blockdiagram of equipment.

The present paper deals with results of evoked response audiometry during sleep in comparison with those obtained from behavioral technique using conditioned orientation reflex (COR) audiometry for young children under five years of age.

METHOD

Subjects

The study comprised 47 normally hearing children aged 4 months through 4 years and 133 hard of hearing children between 1 and 5 years of age. The normal subjects were presumed to have normal hearing in both ears by their histories and otoscopic findings. All of the hard of hearing subjects came from the Speech and Hearing Clinic of the Department of Otolaryngology of Shinshu University Their mental development was tested previously by using nonverbal techniques and proved to have intelligence quotients not worse than 85.

Equipment

The equipment used for recording the evoked response is shown by the block diagram in Fig 1 Tone bursts at frequencies 500 1000 2000 and 4000 Hz were used as stimuli. They had a 25 msec rise and fall time and a 100 msec duration The tones were led to one of the subjects ears by earphones (Iwasaki AH 801) at intervals of 5 sec. The reference levels of the test tones were calibrated by 10 normally hearing young adults. Each series of responses was averaged by means of an analog type computer (San Ei AR 201) and the averaged responses were read out on an oscilloscope (Iwasaki SS 5022). Original EEG pattern was recorded on an ink writing recorder for determining subject's sleep stage In the majority of cases 30 responses were averaged during a test run

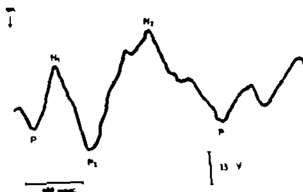


Fig. 2. Typical pattern of averaged evoked response from 3-year-old girl to 30 presentations of 1000 H tone at 30 dB bove her subjective threshold during sleep stage 3. Upward deflection indicates negativity t active electrode.

Procedure

The subjects were sedated with an intramuscular injection of 3 mg per kg of pentobarbital sodium and laid on a bed in a sound proof room. Following onset of sleep, active electrode was fixed at the vertex (Cz), reference electrode at the right mastoid area and ground electrode at the forehead.

The tone stimulus was first given at an intensity above estimated threshold level of the ear under test. If a clear response was recorded the intensity was reduced by 10 dB steps until the response was no longer visualized. Since the most prominent evoked response to auditory stimulus was obtained in sleep stages 3 and 4 of the classification by Dement and Kleitman (1957) (Suzuki et al. 1968 Weitzman et al. 1965), the recording was made in these stages.

Criteria of the Response

The presence or absence of the evoked response was determined by two or three examiners from the pattern on the oscilloscope. Following criteria were adopted for determining the positive response in sleep stages 3 and 4.

1 The response was judged as positive when its three main com ponenents, i. e. N_1 (first negative deflection) with peak latency of 110 to 180 msec, P_2 of 200 to 300 msec and N_2 of 380 to 550 msec or at least P_2 and N_2 appeared and grew with repetition of the stimulus (Fig. 2).

2 When a response was questionable at a given intensity level, its pattern was compared with that of positive response at 10 dB higher level of stimulation. When a close similarity was found between both patterns, the response was judged as positive (Fig 3). It should be kept in mind that the peak latencies in the response tend to increase

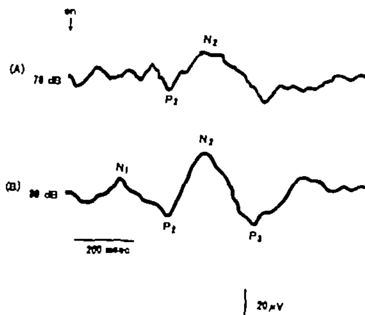


Fig. 3. Averaged evoked response in a girl aged 15 months to 20 presentations of a 1000 Hz tone. The response is questionable at 70 dB SL (A). However by comparing its pattern with that of clear positive response at 80 dB SL (B), the response in 70 dB can be judged as positive.

as stimulating level decreases.

Conditioned Orientation Reflex (COR) Audiometry

COR audiometry is a behavioral testing technique with which pure tone thresholds for young children under three years of age can be measured. Visual orientation reflex is conditioned with pure tones and utilized as index of hearing. For the present study the original method of Suzuki and Ogiba (1961) was used and the hearing thresholds for four frequencies of 500, 1000, 2000 and 4000 Hz were measured in 10 dB steps by a descending technique.

Comparison of ERA and COR

All of the subjects had been tested by COR audiometry prior to being tested by ERA. At the time of performing ERA the examiners were unaware of the results of COR test. Since COR test was made in free field binaurally, evoked response threshold of the better ear was compared with COR threshold of the same frequency.

RESULTS

Normal Subjects

In 5 of the 47 normal children ERA was unsuccessful chiefly because of the failure in maintenance of adequate sleep stages. Table 1 shows the distribution of thresholds by ERA and COR audiometry in the

TABLE 1. *Distribution of evoked response (ER) and COR thresholds for normal children.*

Threshold (dB)	under 1 yr ER	1 yr. ER	1 yr. COR	2 yrs. ER	2 yrs. COR	3 yrs. ER	3 yrs. COR	4 yrs. ER	4 yrs. COR
10			1		6		25		10
20		1	10	5	21	20	25	15	13
30	2	11	5	24	6	26	2	8	1
40	9	13	5	4	1	6		3	
50	7	4		1					
60	3								
Mean (dB)	45.2	36.9	26.7	30.3	21.2	28.3	15.6	25.9	16.3

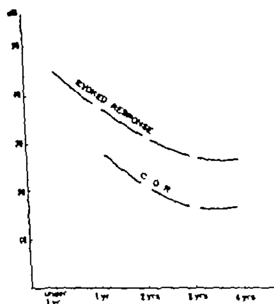


Fig. 4. Mean values of evoked response threshold and COR threshold for normal children in each age group.

remaining 4. children aged 4 months through 4 years. Since no significant difference in the thresholds was found as a function of the frequency of stimulating tones, the data obtained in four frequencies were summed up and presented collectively in a table.

Fig. 4 indicates the variation of mean values of both thresholds as a function of subjects age. Noteworthy is the fact that evoked response thresholds tend to decrease in parallel with COR thresholds as the child becomes older showing the averaged difference of about 10 dB in each age category.

Table – presents the distribution of the difference between evoked response thresholds and COR thresholds. Comparison was made in 131

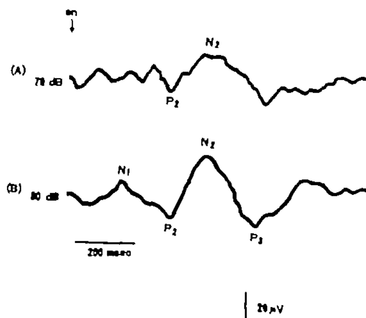


Fig. 3. Averaged evoked response in a girl aged 15 months to 20 presentations of a 1000 Hz tone. The response is questionable at 70 dB SL (A). However by comparing its pattern with that of clear positive response at 80 dB SL (B), the response in 70 dB can be judged as positive.

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COR audiometry is a behavioral testing technique with which pure tone thresholds for young children under three years of age can be measured. Visual orientation reflex is conditioned with pure tones and utilized as index of hearing For the present study the original method of Suzuki and Ogiba (1961) was used and the hearing thresholds for four frequencies of 500 1000 2000 and 4000 Hz were measured in 10 dB steps by a descending technique.

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RESULTS

Normal Subjects

In 5 of the 47 normal children ERA was unsuccessful chiefly because of the failure in *maintenance of adequate sleep stages*. Table 1 shows the distribution of thresholds by ERA and COR audiometry in the

TABLE 4. *Distribution of difference between evoked response (ER) and COR thresholds for severely impaired children (group 2).*

ER−COR (dB)	1 yr.	2 yrs.	3 yrs.	4 yrs.	5 yrs.
−30	1	1			
−20	4	1	3	4	
−10	17	17	17	1	3
0	7	18	19	5	3
10	10	19	17	1	4
20		8	3	2	2

N = 185 M = −0.43 dB SD = 10.90 dB

than evoked response thresholds in normal subjects comes less prominent in group 1 and completely disappears in group 2. The mean difference for gorup 1 is 6.38 dB COR threshold more sensitive, whereas for group 2 it is only 0.43 dB evoked response threshold more sensitive. Statistical investigation of these data including those of normal subjects, revealed that the difference between COR threshold and evoked response threshold diminishes significantly as degree of hearing losses increases.

COMMENT

Early investigators (Suzuki et al. 1962 Appleby et al. 1963 Davis, 1964 McCandless et al. 1964) obtained cerebral evoked response, or vertex potential, with auditory stimulation at 10 dB to 25 dB SL in normal adults. Validating study made by us (Suzuki et al. 1965) showed that the detectable response was obtained in 70 per cent of normal adults with stimulus intensity at 10 dB SL and in 100 per cent at 20 dB SL. McCandless and Best (1966) indicated that the response was seen quite clearly at 10 dB SL in 8 of 10 subjects. Davis (1966) reported the approximate difference between evoked response threshold and behavioral threshold for normal adults ranging from 7.5 to 12.5 dB behavioral more sensitive. McCandless and Lentz (1968) reported that the evoked response measured from 12 normal adults agreed within 5 dB of their voluntary threshold. Price and Goldstein (1966) comapred evoked response threshold and behavioral threshold for 7 normal children. However no numerical evaluation was presented in their paper.

In the present study the evoked response threshold for normal children was pro ed to be approximately 10 dB higher than the be ha ioral threshold for each age category of 1 to 4 years. The results obtained here correspond closely with those in most of the previous reports for normal adults in spite of the difference in the testing technique for the behavioral audiometry. It is of interest that the evoked response thresholds for normal young children decrease successively in

TABLE 2. *Distribution of difference between evoked response (ER) and COR thresholds for normal children*

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0	6	6	3	6
10	6	23	39	13
20	3	5	10	5
30	4			

N = 131 M = 10.38 dB SD = 7.03 dB

pairs of thresholds obtained from 42 children. Again in this comparison the data obtained in four frequencies were combined in a table. The overall distribution of the difference in normal children is almost symmetrical and all but 6 measurements fall within the range between 0 and 20 dB COR threshold more sensitive. The mode is 10 dB and the mean value is 10 38 dB

Clinical Subjects

ERA could not be administered successfully in 11 of 133 hard of hearing children because of failures in the testing procedure. Another 30 severely impaired children showed no response in either ERA or COR audiometry or in both of them even at the maximum intensity level of the stimulating tones. The remaining 92 children aged 1 through 5 years gave a total of 315 pairs of thresholds, which were divided into two groups according to the threshold values for COR test Group 1 consisted of 130 measurements whose COR thresholds ranged between 20 and 60 dB average value being 49 0 dB Group 2 comprised 185 measurements from severely impaired ears with COR thresholds of 70 dB or higher and of 82.9 dB as average.

Table 3 and 4 show the distribution of difference between both thresholds for the above mentioned two clinical groups. As is presented in the tables the trend toward higher sensitivity of COR thresholds

TABLE 3. *Distribution of difference between evoked response (ER) and COR thresholds for slightly or moderately impaired children* (group 1).

ER–COR (dB)	1 yr	2 yrs.	3 yrs.	4 yrs.	5 yrs.
−10	1	3	6	9	–
0	–	3	11	6	10
10	–	4	13	15	11
20	1	3	–	7	9

N = 130 M = 6.38 dB SD = 9.98 dB

TABLE 4. *Distribution of difference between evoked response (ER) and COR thresholds for severely impaired children (group 2).*

ER−COR dB)	1 yr	2 yrs.	3 yrs.	4 yrs.	5 yrs.
−30	1	1			
−20	4	1	3	4	
−10	17	17	17	1	3
0	7	18	19	5	3
10	10	19	17	1	4
20		6	3	2	2

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than evoked response thresholds in normal subjects comes less prominent in group 1 and completely disappears in group 2. The mean difference for gorup 1 is 6.38 dB COR threshold more sensitive whereas for group 2 it is only 0.43 dB evoked response threshold more sensitive. Statistical investigation of these data, including those of normal subjects, revealed that the difference between COR threshold and evoked response threshold diminishes significantly as degree of hearing losses increases.

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ER−COR (dB)	1 yr	2 yrs.	3 yrs.	4 yrs.	5 yrs.
−10	1	3	6	9	2
0	2	3	11	8	10
10	7	4	13	15	11
20	1	3	7	7	9

N=130 M=6.38 dB SD=9.96 dB

TABLE 4. *Distribution of difference between evoked response (ER) and COR thresholds for severely impaired children (group 2).*

ER−COR (dB)	1 yr.	2 yrs.	3 yrs.	4 yrs.	5 yrs.
−30	1	1			
−20	4	1	3	4	
−10	17	17	17	1	3
0	7	18	19	5	3
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20		6	3	3	2

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than evoked response thresholds in normal subjects comes less prominent in group 1 and completely disappears in group 2. The mean difference for gorup 1 is 6.38 dB COR threshold more sensitive, whereas for group 2 it is only 0.43 dB evoked response threshold more sensitive. Statistical investigation of these data, including those of normal subjects, revealed that the difference between COR threshold and evoked response threshold diminishes significantly as degree of hearing losses increases.

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0	–	3	11	8	10
10	7	4	13	15	11
20	1	3	7	7	9

N = 130 M = 6.33 dB SD = 9.98 dB

30 Mitteilungen. Gemäss der Klassifizierung von Dement und Kleitman wurde die Prüfung im Schlafstadium 3 und 4 durchgeführt. Beim Orientierungsreflex Verfahren wurde der Originalmethode von Suzuki und Ogiba gefolgt.

Bei normalen Kindern erreichte der mittlere U terschied zwischen den beiden Schwellen 10.38 dB, dabei war die Empfindlichkeit der "COR" Schwelle grösser und 90.2 Prozent der Messungen bewegten sich im Bereiche von 0 bis 20 dB. Bei Kindern mit einer geringgradigen oder mittelgradigen Schwerhörigkeit nahm der mittlere Unterschied bis zu 6.38 dB ab, dabei war die Empfindlichkeit der "COR" Schwelle grösser Bei den hochgradigschwerhörigen Untersuchten betrug der mittlere U terschied nur 0.43 dB, wobei aber die evozierten Erregungsantworten empfindli cher waren. Ein signifikant kleinerer U terschied zwischen der durch das Mittel ungsverfahren bestimmten Schwelle evozierter Erregungsantworten und der "COR" Schwelle wurde eher bei schwerhörigen Kindern als bei normalhörenden Kindern statistisch erwiesen.

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parallel with the behavioral thresholds as the subjects age increases.

For hard of hearing children the relation between evoked response threshold and behavioral threshold is quite different from that for normal subjects. Rapin (1964) compared evoked response threshold and subjective threshold on 36 children with hearing losses of 50 dB or higher and one child of normal hearing In 19 of 37 children the two thresholds were within 10 dB of each other In 23 of 37 instances the evoked response was more sensitive than the subjective threshold

Davis and associates (1965 1966 1967) also made such a comparison in 162 hard of hearing children aged 4 through 15 years. The average difference was only 0 9 dB subjective response more sensitive. In 119 of the 162 cases the difference fell within 7 5 dB Other reports (McCandless, 1967 McCandless et al 1968 Theissing 1967) indicated almost the same results.

Our present findings in hearing impaired children aged 1 to 5 years correspond closely to the above mentioned data and confirmed that significantly closer approximation of the evoked response threshold to the behavioral threshold occured in subjects with hearing impairments than in normal subjects. The cause of this discrepancy between normal and impaired subjects is not clear Rapid development of loudness in the ear with sensori neural defects may play a causal part in this discrepancy

Though there is no theoretical necessity for exact agreement between evoked response threshold and volunatary threshold it is practically of great convenicence for estimating the hearing acuity of young children with evoked response audiometry

ACKNOWLEDGMENT

We wish to extend our thanks to Dr J A. Orpin for his careful review of the manuscript and to Dr E. König for preparing German summary

ZUSAMMENFASSUNG

Die durch das Mittelungsverfahren bestimmten Schwellen evozierter Erregungsantworten auf akustische Reize bei schlafenden kleinen Kindern wurden mit den durch das Verfahren der Konditionierten Orientierungsreflexe ("COR. conditioned orientation reflex") ermittelten Schwellen verglichen 47 normalhorende Kinder im Alter zwischen 4 Monaten und 4 Jahren sowie 133 schwerhorige Kinder im Alter zwischen 1 und 5 Jahren wurden geprüft. Davon waren die Prüfungsergebnisse von 42 normalhörenden und diejenigen von 92 schwerhörigen Kindern zum Vergleich zugänglich. Die Registrierung der evozierten Erregungsantworten erfolgte bei Verwendung von Sinustonimpulsen, deren Frequenz 500 1000 2000 und 4000 Hz betrug Diese 100 ms dauernden Sinustonimpulse hatten eine An und Abklingzeit von 25 ms und wurden alle 5 Sekunden dargeboten Im Verlauf einer Untersuchungsreihe beruhte die Identifizierung der evozierten Potentiale auf ungefähr

Acta oto-laryngologica Supplementum 252, 29-36 (1969)

HUMAN FETAL EVOKED RESPONSE TO ACOUSTIC STIMULATION

N. SAKABE, T. ARAYAMA and T. SUZUKI

From the Department of Otolaryngology, Faculty of Medicine, Shinshu University, Matsumoto, Japan

Human fetal evoked response to acoustic stimuli was recorded from the abdominal wall of six mothers at the 32th to 38th week of pregnancy. Tone bursts with frequency of 1000 Hz, duration of 50 msec, and rise and decay time of 13 msec were given every 4 seconds through a bone vibrator attached to the maternal abdominal wall at the nearest place to the fetal ear. The responses were conducted through an active electrode located on the maternal abdominal wall in the vicinity of the fetal vertex and were averaged by a digital computer.

The typical wave form of the response consisted of four prominent deflections: negative, a positive, a negative and a positive deflection with respective peak latencies of 100 to 150 msec, 200 to 300 msec, 500 to 600 msec and 700 to 800 msec. These deflections of the fetal evoked response were considered to correspond to the four components (N_1, P_2, N_2, P_3) of the slow "vertex potential" to auditory stimulus in young children. However, the decision can not be reached as to whether the response obtained in the present study is originated in the fetal brain and depends on the fetal auditory function.

Recently the cerebral evoked responses to acoustic stimuli in new born infants and young children can be detected easily by averaging the responses using electronic computers. The method has already been well established and applied to audiometric purposes. However, little has been written on the cerebral evoked responses to acoustic stimulation in fetuses and no attempt has been reported on the fetal evoked response recorded with electrodes attached to the abdominal wall of a pregnant woman. The present paper is a preliminary report of our study on the recording of the fetal evoked response to tonal stimulation by the abdominal leads with the hope of developing a method for detecting hearing defects of a child during its fetal life.

METHOD

Subjects

Six healthy mothers at the 32th to 38th week of normal pregnancy were selected for the investigation. Their fetal heads were located on

Theissing, J. 1967: Über Beziehungen von Computeraudiogrammen und konventionellen Audiogrammen. Z. Laryng. Rhinol. 46, 455.
Weitzman, E. D. and Kremen, H. 1965: Auditory evoked responses during different stages of sleep in man. Electroenceph. Clin. Neurophysiol. 18, 65.

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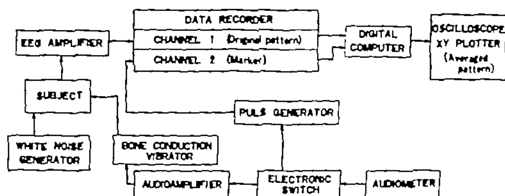


Fig. 1 Blockdiagram of equipment.

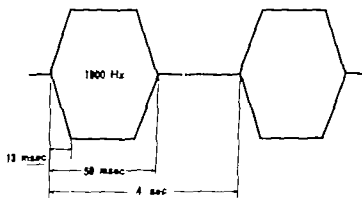


Fig. 2. Interval, duration and rise and decay time of stimulating tone.

the pelvis of the mothers and protruded in the lower part of the hypogastrial region.

Equipment and procedure

The block diagram of the equipment used for the present study is shown in Fig. 1. The acoustic stimulus used was a tone burst with frequency of 1000 Hz, duration of 50 msec. and rise and decay time of 13 msec (Fig. 2). The stimulus was given every 4 seconds through a bone conduction vibrator (Rion BCR 4) fixed closely to the skin of the maternal abdomen at the nearest place to the fetal ear (Fig. 3). The vibration amplitude of the vibrator was calibrated with an accerelometer and fixed at 50 microns throughout the present investigation. However, the actual intensity of the stimulating tone which is delivered to the fetal ear could not be measured.

Electrodes were placed on the median line of the abdominal wall of the mothers. As shown in Fig. 3, an active electrode was fixed at the nearest place to the fetal vertex, while a reference electrode was attached to the fetal cervical region.

Original waves were examined previously with an oscilloscope so as to avoid the mixture of maternal ECG and artifacts. Original res-

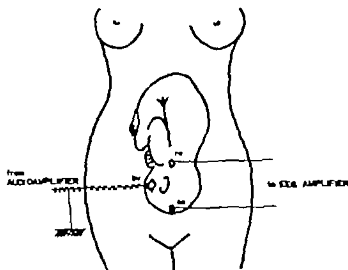


Fig. 3. Schematic representation of position of electrodes and bone conduction vibrator. re = reference electrode ac = active lectrode bv = bone conduction vibrator

ponses and signals of the stimulus were recorded separately on two channels of a data recorder (San'Ei AR 201) and a subsequent averaging was carried out by means of a digital computer (San'Ei MC 401). Averaging number ranged from 80 to 100.

As a rule the maternal ears were masked with a white noise of sufficient intensity during the examination.

RESULTS

Averaged evoked responses of a characteristic wave form were obtained using electrodes placed on the maternal abdominal wall. As shown in Fig. 4 and 5, typical wave form of the evoked response consists of four successive deflections. The initial negative deflection (N_1) is seen at approximately 100 to 150 msec from the onset of the stimulating tone. Next positive deflection (P_1) at 200 to 300 msec is followed by a negative deflection (N_2) at 500 to 600 msec and a later positive deflection (P_2) with peak latency of 700 to 800 msec. Not all peaks were clearly obtained in all responses. Noted is that P_1 and N_2 were recognized in all subjects examined while N_1 and P_2 were equivocal or absent in some cases. Of course such time locked deflections could not be observed in records obtained from the maternal abdominal wall when no acoustic stimulation was presented (*Fig. 6*).

Fig indicated a comparative observation on the averaged evoked response to auditory stimulation in a newborn baby who was born prematurely at the 5th day of the 37th week of pregnancy. The response

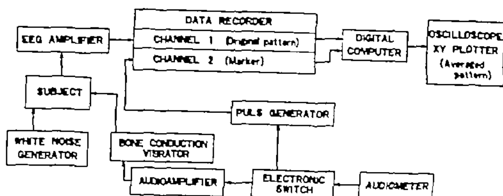


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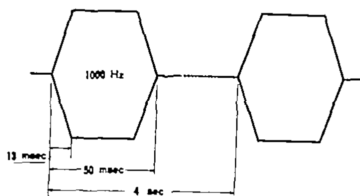


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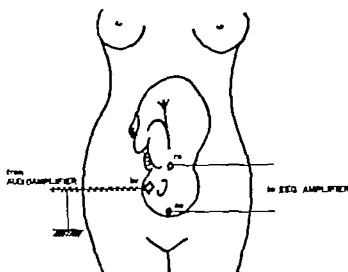


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Fig. 7 indicated a comparative observation on the averaged evoked response to auditory stimulation in a newborn baby who was born prematurely at the 5th day of the 37th week of pregnancy The response



Fig 4. A typical evoked response to acoustic stimlus recorded from a maternal abdominal wall at the 36th week of pregnancy Four successive deflections are observed.
Stimulus 1000 Hz tone burst Vibration amplitude: 50 μ Averaging number 90

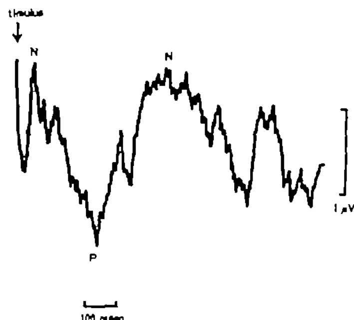


Fig 5. Evoked response to acoustic stimulus recorded from an another maternal abdominal wall at the 36th week of pregnancy The component P i equivocal
Stimulus 1000 Hz tone burst Vibration ampl tude 50 μ A eraging numbe 90

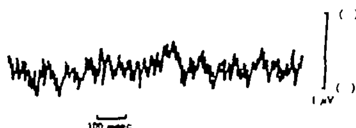


Fig 6. Averaged wave from the same subject wher the acoustic stimulus i not gi en.

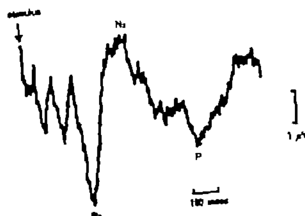


Fig. 7. Averaged evoked response to acoustic stimulus recorded from the vertex of newborn baby who was born prematurely at the 6th day of the 37th week of pregnancy. Components P N and P are clearly observed.
Stimulus: 1000 Hz tone burst. Intensity: 85 dB SPL. Averaging number: 30.

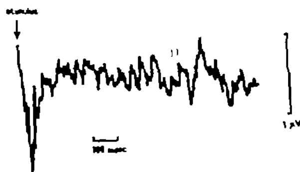


Fig. 8. Averaged wave from the abdominal wall of a non-pregnant woman. Tone stimulus was gi en in the same way as shown in Fig. 4 and 5.

was recorded 8 hours after birth from the vertex of the baby's scalp with stimulating tone of 1000 Hz at the intensity level of 85 dB SPL given through a speaker placed at 20 cm from the baby's head. A close similarity was found in the patterns between the fetal evoked response and that in the newborn baby.

Fig. 8 shows an averaged wave recorded from the abdominal wall of a normal non pregnant woman to whom the acoustic stimulation was given in quite the same way as it was given to the pregnant subjects. The wave was flat and no evoked response was detectable. The initial deflections in the wave were an artifact due probably to a leakage of the stimulating tone.

COMMENT

The fetal reactivity to acoustic stimulation was first reported by Peiper in 1924 He observed changes in the fetal movement in response to intense sound stimulation in a fetus of 40 weeks of age Recent investigations indicated that the fetus in the third trimester of intra uterine life reacted to acoustic stimuli by changes in the fetal movement and heart rate (Bernard et al 1947 Fleischer 1955 Murphy et al 1962 Johanson et al. 1964 Dwornicka et al 1964 Smyth et al 1967).

Lindsley (1942) recorded the fetal brain potential in a fetus of 7 months of age with electrodes placed on the maternal abdominal wall Okamoto and Kirikae (1951) observed the electrical activity of the fetal brain as early as 6 weeks of age. More recently several investigators recorded the fetal EEG using scalp vaginal or abdominal electrodes and endorsed the existence of the electrical activity in the human fetal brain (Bernstine et al 1955 Borkowski et al. 1955 Rosen et al 1965).

Hon et al. (1967) recorded the fetal evoked response to acoustic stimuli with the purpose of investigating the fetal physiological state during delivery by comparing the changes in the evoked response with those in the heart rate. They attached two electrodes to the fetal vertex which entered into the birth canal during labor and presented acoustic stimuli to the fetus by inserting an earphone near one of the fetal ears Averaging technique was utilized for recording the evoked response The authors claimed that there are definite wave forms which bear a temporal relationship to the stimulus. When the fetus was in normal status typical triphasic patterns of the auditory evoked response were observed. Barden et al (1968) also attempted to record the fetal auditory evoked response with fetal scalp electrodes. They obtained the evoked response in one of six subjects. The response appeared to be similar in wave form to the auditory evoked response in newborn babies

All the above mentioned studies imply us a strong possibility of the existence of the auditory evoked response in the fetal brain which corresponds to that obtained from the vertex of newborn babies. The present study revealed that an averaged evoked response to acoustic stimuli could be recorded with electrodes placed on the abdominal wall of pregnant mothers. Four successive deflections observed in the fetal evoked response appeared to correspond closely to the four components (N_1 P N_2 P_2) of the averaged evoked response, or vertex potential" to auditory stimulation in newborn children (Goodman et al. 1964 Weitzman et al 1965). The response did not appear without

tonal stimulation, nor was it obtained unless the active electrode was placed in close proximity to the fetal vertex even though the stimulus was given. It could not be recorded from the abdominal wall of non pregnant woman.

From the method used in the present study and the results obtained, there can be little doubt that the response obtained is a fetal response. However problems still remain with reference to the nature of the response and it is impossible at the present time to decide whether the response is elicited from the fetal brain with the stimulus conducted through the cochlea. The study will be further extended to improve testing technique and to investigate the clinical value of the response.

ACKNOWLEDGMENT

The authors wish to extend their thanks to Dr J. A. Orpin for the careful review of the manuscript and to Dr E. Konig for German translation.

ZUSAMMENFASSUNG

Evozierte Erregungsantworten auf akustische Reize beim menschlichen Fetus wurden bei 6 Müttern an der abdominalen Wand im Zeitpunkt zwischen der 32. und der 38. Woche der Schwangerschaft registriert. Sinustonimpulse mit einer Frequenz von *1000 Hz*, einer Dauer von 50 ms und einer An und Abklingzeit von je 13 ms wurden alle 4 Sekunden durch einen an der mütterlichen abdominalen Wand möglichst nahe beim Ohr des Fetus fixierten Knochenvibrator dargeboten. Die evozierten Erregungsantworten wurden über eine sich auf der mütterlichen abdominalen Wand in der Nähe des Scheitels des Fetus befindliche aktive Elektrode geleitet und mit Hilfe eines Digital Computers ausgemittelt.

Der typische Wellenverlauf der evozierten Erregungsantworten bestand aus vier ausgeprägten Auslenkungen einer negativen, einer positiven, einer negativen und einer positiven Auslenkung mit Spitzenlatenzen von 100 bis 150 ms, 200 bis 300 ms, bzw von 500 bis 600 ms und 700 bis 800 ms. Diese Auslenkungen der evozierten Erregungsantworten des Fetus betrachtet man als den vier Komponenten (N_1, P_1, N_2, P_2) des evozierten langsamen "Vertex Potentials" auf akustische Reize bei kleinen Kindern entsprechend. Es kann jedoch keine Entscheidung getroffen werden, ob die in diesen Untersuchungen ermittelten evozierten Erregungsantworten im Gehirn des Fetus entstehen und von der Gehörfunktion des Fetus abhängen.

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COCHLEAR MICROPHONIC RESPONSES TO PURE TONES IN MAN RECORDED BY A NON SURGICAL METHOD

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A non surgical method of recording the cochlear microphonic (CM) responses in man has been developed, using new active electrodes in combination with an verage response computer One of these electrodes was needle electrode placed in the external acoustic meatus, another a fine 80-micron stainless steel wire electrode associated with a special cannula, which was placed on the promontory or the round window niche.

The procedure of the electrode placement was carried out completely without pain or bleeding The acoustic stimuli were continuous pure tones or short bursts of pure tone. Subjects were volunteers with normal hearing and patients with conductive and sensorineural hearing loss. All the procedures of this experiment were made in sound proof room.

The results are condenced into the following

(1) All the subjects with normal hearing showed consistently and stably the cochlear microphonic response, recorded either from the external acoustic meatus or from the promontory

(2) When the short bursts of pure tone were presented, complex response consisting of cochlear microphonic, action potential (AP) and summating potential (SP), was recorded from the promontory and a complex response of the cochlear microphonic and action potential was recorded from the external acoustic meatus.

(3) When the continuous pure tones were presented, beautiful records of the cochlear microphonic responses were obtained both from the external acoustic meatus and from the promontory

(4) The form of the intensity function measured from the promontory in the normal subjects was in essential agreement with that reported for the round window recording in animals.

(5) Some of the intensity functions obtained from patients with severe sensorineural hearing loss showed the following abnormal patterns (a) reduction in the magnitude of the cochlear microphonic response, (b) distortions in the form of the intensity function (the nonlinear relation), and (c) parallel shift of the intensity function to the right side (reduced sensitivity).

(6) The sensitivity of the cochlear microphonics seemed to have some relation to the degree of the hearing loss in the audiogram.

(7) The non surgical method is pplicable to routine clinical udiometry for differential diagnosis of sensorineural deafness, but empirical correlations must be established between the form of intensity functions and different types of sensorineural deafness.

(8) In middle ear impairment the less sensitive extratympanic method must be employed and the cochlear microphonics do not offer any advantages over other audiometric and otologic methods of diagnosis.

INTRODUCTION

From researches on cochlear electrophysiology in animals it is well known that an extracochlear electrode placed on the round window membrane of the animals can pick up three different electrical responses to acoustic stimuli from the cochlea viz. 1) the cochlear microphonics (CM), 2) the summating potentials (SP), and 3) the whole nerve action potential responses of the cochlear nerve (AP).

If one would hope for clinical use of these cochlear responses in man according to the higher demands of clinical audiometry the practical problem of electrodes suitable for clinical use should be completely settled

The history of the study of human cochlear responses began with a number of early works carried out by Fromm et al (1935), Andreev et al (1939), Perlman & Case (1941), and Lempert et al (1947 1950). They could record the CM with a gross electrode placed on the round window membrane by a surgical approach during operations on the ear They observed that the round window membrane was the only suitable location for the electrode and it is possible to record the CM without major surgical procedure only in those rare instances in which the anatomic conditions are favorable. Unfortunately they could not demonstrate consistent cochlear responses that could be used routinely for objective audiometry It was concluded after these considerable efforts that the recording of the CM in man was not a practical clinical procedure (Lempert et al 1950). In view of the technical difficulty in obtaining a consistent response in man it is not surprising that the matter has not been considered in clinical otology since these early researches on the human CM

During recent years the introduction of newly developed instruments for biomedical use consisting of a low noise high gain biomedical amplifier a precise acoustic stimulator and a multichannel FM data recorder by Ruben and his colleagues (1959 1960), has permitted the stable and consistent recording of the CM and AP in man from an electrode placed on the round window and an application of this surgical techinique by them (1961 1962, 1964 1967) has furnished us with a beautiful series of records illustrating changes in these cochlear responses (CM and AP) associated with various types of hearing loss. Ronis (1966), using the surgical method first applied a computer technique of averaging or summation to the measurements of the CM and AP in man These results will be discussed later in this paper Very few other reports in the literature dealt with the same problem (Krejci

et al 1949 1950 Brinkman & Tolk, 1961/1962 Flach & Seidel 1968), but Flach & Seidel (1968) reported the most extensive findings on the human CM in conductive deafness. In summary as long as surgical methods are employed there is a limitation of clinical application because a clinical routine test must be simple in practice as well as reliable and accurate in results. The operative procedure seems quite inadequate for systematic investigations on the human cochlear responses.

As regards the non surgical recording of the human CM, the first description as far as we know is found in the report of Lempert et al (1950), which was reviewed only briefly above. They passed a needle electrode through the tympanic membrane and made it contact closely with the bony promontory beyond the tympanic membrane. According to them, after the needle was withdrawn the tympanic membrane healed perfectly in a short time. The results with the CM were much inferior to the ones obtained with surgical placement on the round window membrane.

The second report was made by Gavilan et al (1964), using a high gain amplifier with sharply selective filters. They recorded the CM in man by an electrode placed on the tympanic membrane. Such a method was likely not only to need a great deal of skill in fixation of the active electrode on the tympanic membrane, but also to be much troubled with interferance of a pseudo CM caused by the induction phenomenon of alternating current flow in the acoustic stimulating system.

These results in the non surgical recording of the CM did not meet the clinical requirements for practical use. The advent of an average response computer allowed a rapid advance in researches of various evoked responses in man (Rosenblith, 1959; Goldstein 1961 Katzman, 1964 Cox, 1965). Hilger et al (1965) first reported a method of recording nonsurgically the CM in cats by means of an average response computer As mentioned above, the first use of the computer techinique for measurements of the human CM was made by Ronis (1966). These averaging or summing methods of recording the CM (an alternating current responses) to periodic acoustic signals (pure tone stimuli) was completely based on the same principle that Miller et al (1964) used to measure extremely small signals with a waveform of periodic variation by a special purpose computer This method can be well applied to the situations where noise interferes with measurements of periodic signals of very low levels in the area of physiological and psychological acoustics, on the basis of the theoretical considerations stated by Miller et al (1964). Although the non surgical method has been established for AP in man by means of an average response computer (Yoshie et al 1967 Yoshie, 1968 Sohmer & Feinmesser 1967 Portmann et al,

1967 1968 Spreng & Keidel 1968), as far as we know we have as yet very little information as to whether such averaging or summing method is valid for the non surgical recording of the human CM

A practical method has been developed for this purpose since 1963 in our laboratory We have obtained nonsurgically these electrical cochlear responses by extracochlear electrodes placed in various regions of the ear in man i.e 1) the CM AP and SP were recorded by an electrode placed on the promontory and 2) the CM and AP were recorded by an electrode placed in the external acoustic meatus. The combined use of the computer and the extracochlear electrode which will be explained later in the following section furnished us the key to non surgical recording

The purpose of this study were (1) to outline the method of recording the human CM (2) to observe various findings on the CM in the normal ear and (3) to demonstrate changes in the CM from patients with various types of hearing loss.

METHODS

The general outline of this experimental method was essentially the same as that of Hilger et al (1965) and Ronis (1966), except for the following minor modifications 1) an application of new extracochlear electrodes and 2) a versatile arrangement of the recording and stimulating equipments. We shall describe the steps of this method and a number of technical precautions necessary for the procedure.

Subjects

A total of 10 subjects with normal hearing and 30 patients with hearing loss of various types ranging in age from about 15 years old to about 65 years old were examined in respect to one or two of cochlear responses (CM and AP) by the non surgical method Before these responses was recorded from them clinical otological examinations, such as otoscopic examination roentogenography audiologic routine tests and so on had been employed

Apparatus

A simplified block diagram of all the apparatus is shown in Figure 1 The arrangement is classified into three systems, viz. 1) a stimulating system 2) a recording system and 3) a synchronising system of stimulation with responses.

The stimulating system is subdivided into 1) a pure tone generator and 2) a transient signal generator as illustrated in Figure 1 The former can produce two types of pure tone signals consisting of continuous sine waves and short bursts of sine waves. These signals can

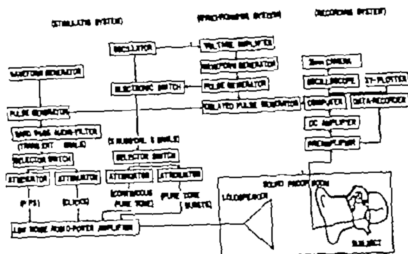


Figure 1. Block diagram showing arrangement of stimulating, synchronising, and recording apparatus.

be presented alternatively by a change over switch. The latter can produce two types of transient signals consisting of clicks and pips (filtered clicks), either of which can be selected by the change over switch. The pure tone generator was employed exclusively in this study because the main purpose of this experiment was to obtain the CM response to pure tone stimuli in man. The transient signals were preferable for recording the AP as has been reported (Yoshie et al, 1967).

The recording system comprised six components, as shown in Figure 1; an AC amplifier (SAN'EI MPA 203 TOKYO) with a flat frequency response curve over the frequency range 30 Hz to 1000 Hz, a DC amplifier (SAN'EI, MPA 203, TOKYO), an average response computer (SAN'EI MEDIAC 401 TOKYO), an oscilloscope (IWASAKI DS 5014 TOKYO), an X Y recorder (TOA DENPA XYR 1A, TOKYO), and photographing equipment for 35 mm films (CANON MODEL IV TOKYO). The computer was used "on line" for averaging or summing the sample waveforms from the output of the biomedical amplifier system, with a "window" or analysis time of 31.25 msec, and with a summing or averaging number of 500 responses. Unfortunately the computer could not follow "on line" the CM at high frequencies above 2000 Hz. The CM responses were limited to a frequency range from 500 Hz to 1000 Hz in this experiment. The computer was triggered by a train of trigger pulses which were generated from the synchronising system in Figure 1. The triggering interval was taken at a period of 50 msec for recording the CM to the continuous tones and at a period of 200 msec for the short tone bursts. The summed or averaged waveforms of these responses

were displayed on the oscilloscope, and then these results were photographed on 35 films or written out on the X Y recorder immediately The potential changes at the tip of the cochlear electrodes were introduced to the AC amplifier with a voltage gain of 1000 fold The output of the amplifying system was connected to the computer as described above

The synchronising *system which plays the most important role in* the function of the summing or averaging computer system comprised four instruments a waveform generator (NIHON KOHDEN SW 1 TOKYO), a pulse generator (NIHON KOHDEN SP 1 TOKYO), a delayed pulse generator (NIHON KOHDEN SD 1 TOKYO), and a voltage amplifier as shown in Figure 1 In short this system produced the trigger pulses by which the computer could be driven in phase, correlating with the waveform of sine wave acoustic signals Therefore, the sinusoidal waveform of the CM to sine wave tones could be summed up or averaged in phase More detailed considerations on such correlating or synchronising system are available in earlier reports (Miller et al 1964 Hilger et al 1965 Ronis, 1966).

Acoustic Stimulation

The sound was presented by means of an open acoustic system in which a driver unit with a frequency range from 200 Hz to 4000 Hz served as an electro acoustic transducer The driver unit was shielded completely to avoid electro magnetic interference with the recording system It was located 30 cm lateral to the ear of the subject on the side of being tested The frequency of the acoustic signals was limited to a range from 500 Hz to 1000 Hz, being varied by 100 Hz steps, because the frequency range of the computer was below 2000 Hz. The intensity of the signals was represented by the sound pressure level (in dB relative to 0 0002 dyne/cm²), which was measured with a calibrated condenser microphone connected to the sound level meter The microphone was placed in similar position at 33 cm distance from the loudspeaker to the tympanic membrane of the subject in order to monitor the acoustic waveform The intensity of the stimulus was controlled over a 100 dB range divided in 1 dB steps by adjusting a manually operated attenuator The signals were given continuously or interruptedly The tone bursts of variable duaration were obtained by passing the continuous pure tone signals through an electronic switch as shown in Figure 1 Usually these signals were presented under conditions of a duration of 25 msec and a rise decay time of 5 msec or 10 msec.

Figure 2 shows the summed waveform of the two types of pure tone stimuli which were recorded from the output of the sound level meter in combination with the condenser microphone These summed

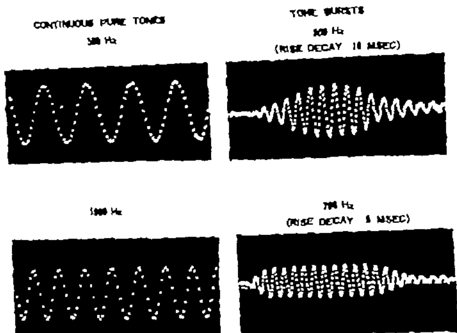


Figure 2. Summed wa eforms of acoustic signals. Each of the traces is an example of summing 100 sample w eforms f om the output of the sound level meter connected with condenser microphone.

sinusoidal waveforms are quite the same as single sample waveforms of the original tone stimuli. These records may be taken as guides for the pattern of summed response of the CM to the pure tone stimuli.

Electrodes

Two types of active electrodes were used for the extracochlear recording of the human CM AP and SP One was a needle electrode with polyethylene coating except at the tip which was placed on the e ternal acoustic meatus near the annulus tympanicus. Another was a polyurethane coated stainless steel wire, 80 microns in diameter which was placed on the promontory after the tip of the wire was passed through the tympanic membrane. Hereafter the terms "extratympanic" and intratympanic will be used synonymously with external acoustic meatal and promontory for convenience. The indifferent electrode was a disc electrode held in place on the ear lobe or on the mastoid region with electrolyte jelly

1) The extratympanic electrode

The electrode of this type has been described in detail elsewhere (Yoshie et al. 196‾ Yoshie 1968). Usually after local infiltration anesthesia with 1 or ~ Citanest* Adrenalin mixture, the electrode

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soldered with a fine leading off copper wire for grounding at its basal end. The flange formed by the polyethylene drop serves to control the depth of the tip of the cannula and also to withstand sudden and large movements of the wire electrode when the cannula penetrates through the tympanic membrane into the tympanic cavity Complete insulation should be maintained between the wire electrode and the hypodermic needle cannula.

The procedure for placement of the intratympanic electrode was divided into two steps. The first steps was fixation of the cannula on the tympanic membrane. The same local infiltration anesthesia as described earlier was performed The cannula was inserted in the posterior region of the pars tensa preferably at the marginal portion of the tympanic membrane up to the depth of the flange. There was suggestive evidence that the electrode might be located anywhere on the promontory at least near the round window niche The magnitude of the CM response was large, sometimes strongest at this particular position of the tympanic membrane. This procedure was done under otoscopic inspection with an usual ear speculum, which was withdrawn from the external acoustic meatus after the insertion of the cannula on the tympanic membrane. The cannula was bonded firmly to the edge of the tragus with a strong adhesive

The second step was to place the wire electrode on the bony promontory near the round window niche, passing through the cannula. The wire electrode could be run easily against the bony wall of the promontory by inserting it through the hole of the cannula inwards. After making close contact with the promontory the wire electrode was bonded firmly to the basal end of the cannula with the same adhesive Finally the leading off wire of the electrode was connected to an input terminal of the AC preamplifier in combination with the indifferent electrode The cannula of course was grounded

In summary with regard to difficulties in practice, we believe anyone with only a little skill in paracentesis or myringotomy could make ll these steps of the procedure without any uncomfortable accident to the patient. In our experience the patients have not complained of pain or bleeding in the ear during the procedure. In addition the perforation of the tympanic membrane healed in a very short time without any complications. It was not a task which called for much skill.

Proced res

The subject lay urpine on a bed which was placed in an electrically shielded sound proof room under comfortable conditions of temperatu and humidity He was instructed to avoid unnecessary movements of the head and to remain relaxed du ing the series of acoustic

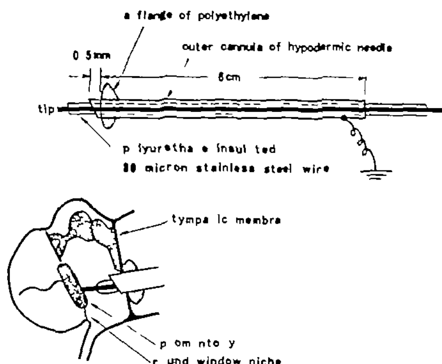


Figure 3. Schematic diagram of the intratympanic electrode

was placed in position on the posterior wall of the external acoustic meatus as medially as possible to the tympanic membrane. It was stuck firmly to the outer edge of the tragus with a strong bonding agent

2) The intratympanic electrode

Figure 3 illustrates a new intratympanic electrode which has been developed to allow continuous recording from the promontory for the time necessary for a series of these tests. In addition the electrode affords great facility for applying these cochlear responses (CM, AP and SP) to a routine clinical hearing test without any complicated surgical procedure. The basic structure of the electrode consists of a very fine stainless steel wire electrode which is insulated with a thin polyurethane coating and has a diameter of 80 microns, and a special outer cannula made of a hypodermic needle of about 6 cm in length and of 0.3 to 0.4 mm in diameter. The polyurethane coating is scraped in the region of 500 microns or slightly less at the tip of the wire electrode. A fine leading off copper wire, about 6.0 cm in length is soldered at the basal end of the electrode. Such a wire electrode enters the cannula through its basal end and then proceeds to the tip of the cannula until the tip of the wire electrode makes close contact with the promontory. The cannula is provided with a small flat drop of polyethylene at the distance of 0.5 to 1.0 mm from its tip. The polyethylene drop is formed by melting a short fragment of polyethylene tubing on the hypodermic needle. In addition the cannula is

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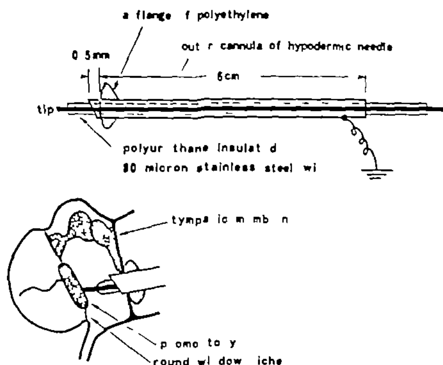


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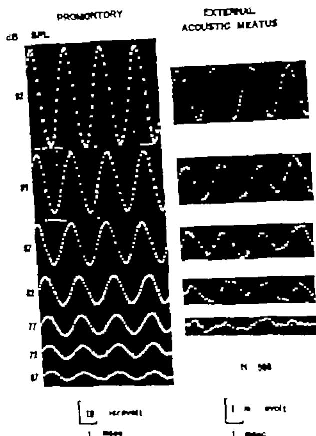


Figure 4. The CM responses to 500 Hz pure tone i man recorded both from the external acoustic meatus and from the promontory The pure tone stimuli were given continuously All the traces show the summed waveforms of summing 500 sample responses. In this and the following figures upward deflection indicated negativity of the meatus or the promontory with respect to the reference electrode The subject was 25-year-old male, with normal hearing. All the summed responses were photographed on the face of cathode ray oscilloscope.

reported for animals (cf Stevens & Davis, 1938 Davis, 1951 Wever & Lawrence, 1954) and for human beings (Ruben et al 1959 1960 1961 Ronis, 1966).

The waveform of the CM response was distorted in a great degree at the low intensity of the stimulus, near a pseudo threshold or a detection threshold which has been discussed by several authors Stevens & Davis, 1938 Davis, 1957 Wever 1959 1966 McGill, 1959 by the contamination of background noise, as shown in Figure 4 As a rule the background noise interfered much more with the wave form of the CM response obtained by the extratympanic electrode than that obtained by the intratympanic electrode The distortion of

stimulating runs. Short bursts of pure tone were delivered at an interval of 200 msec, and the responses to 500 tone bursts were summed "on line" in one run. In the case of continuous tone stimuli the responses were sampled every 50 msec by the computer and 500 sample responses were summed in one run. After all, summing the responses to 500 stimuli in one run took 100 sec for the tone burst signals or 25 sec for the continuous tone signals, in addition to which one more minute was used for photographing or writing out the summed response and resetting the apparatus. It took about an hour or slightly more to terminate one series of experimental observations on the CM.

In this experiment, choice between the extratympanic electrode and the intratympanic one was made quite arbitrarily, but the authors intend to use the latter in their future work. The electrode placement was carried out easily in the sound proof room. After fixation of the electrode, the DC resistance between the active and indifferent electrodes was measured. It was reasonable, for stable and consistent recording, that the value of the resistance was lower than 30 kilohms for the extratympanic electrode and lower than 15 kilohms for the intratympanic electrode. It was absolutely necessary, as has been pointed out by Hilger et al (1965), to separate electrically the recording system from the stimulating system completely and to provide good grounds for the shields.

RESULTS

Waveforms

All the subjects with normal hearing have consistently shown CM, AP and SP responses both to the continuous pure tones and to the short bursts of pure tone. These have been recorded both from the external acoustic meatus and from the promontory. The summed wave forms of the electrical cochlear responses to the continuous pure tones were simply sinusoidal and reproduced well the forms of the original acoustic signals, shown in Figure 2. This is convincing evidence that these alternating electrical potential responses as a result of acoustic stimulation of sinusoidal signals were the CM responses in man. Figure 4 shows the summed waveforms of the CM responses in man to the continuous pure tone stimulus, in which the simple sinusoidal form similer to the stimulus is maintained until the intensity reaches the high intensity of some 100 dB SPL. It is obvious from this figure that the magnitude of the CM response continues to increase as the stimulus intensity is increased up to a level of about 100 dB SPL. The quantitative relation of the magnitude of the CM response in man to the stimulus intensity will be described in detail later. These findings on the waveform of the human CM are in good agreement with those

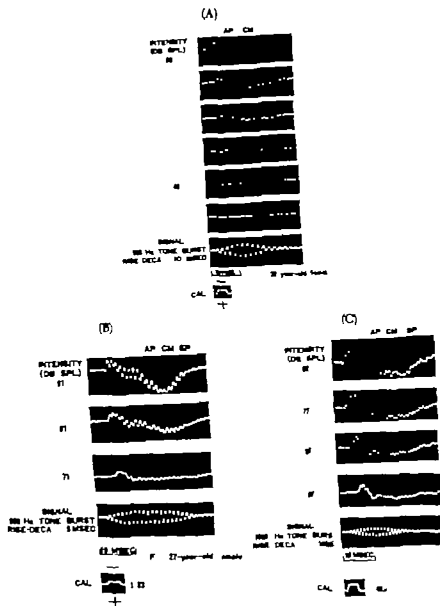


Figure 6. Comple responses to the tone bursts with frequencies of 600 Hz (A), 900 H (B), nd 1000 H (C), recorded from the promontory in man (Y F 27 year-old female), showing the AP and CM (A) or the AP CM and SP (B and C). Each trace i the sum of 500 sample responses.

non surgical recordi gs. In summary at high intensities no or little distortion of the summed waveform was revealed over frequencies from 500 Hz to 1000 H in gross appearance, and at low intensities, in contrast the distortion due to background noise was overwhelming.

On the other hand the waveform of the response to the short

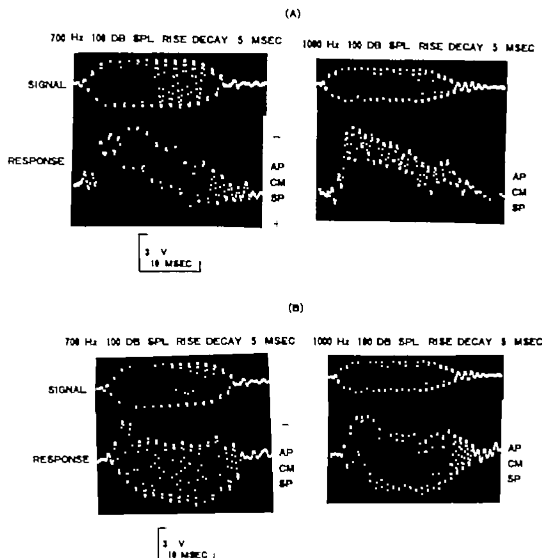


Figure 5. Complex responses to the tone bursts recorded from the promontory of human subjects ((A) S. Z. a 25-year-old male; (B) M. N. a 20-year-old female), showing the CM responses (700 Hz and 1000 Hz), the AP (the peaks and humps superimposed on the rising phase (A) or on the falling phase (B) of the SP response), and the SP response (upward displacement (A) or downward displacement (B) of the base line. Each trace is the sum of 500 sample responses.

the summed waveforms due to the background noise seemed to be the most serious kind of distortion in recording the CM nonsurgically by the computer method of summation. At high intensities, although the highest level was at best about 100 dB SPL, the summed waveforms were quite smoothly sinusoidal without a notch or hump or peak clipping over a frequency range from 500 Hz to 1000 Hz. The waveform distortion caused by the combination of the AP with the CM (*cf.* Stevens & Davis 1938; Wever & Lawrence 1954; Wever 1966) has not been confirmed in this experiment, for reasons we believe of the distortion due to background noise which may be inevitable for the

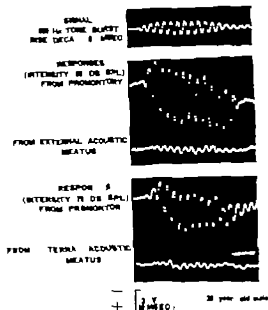


Figure 7 Comple responses recorded both from the promontory and from the external acoustic meatus in man (Y K. 20-year-old male Both the intratympanic electrode and the xtratympanic lectrode were pplied to the subject simultaneously All traces are the sum of 800 sampl responses.

proportions, supporting the view of Davis (1957). Although in order to obtaine pure information exclusively as to the CM response in man the continuous acoustic stimulation by a pure tone is preferable to the short burst stimulation the pattern in response to the latter seems to be available for making an overall estimate of the cochlear electrical responses (CM AP and SP).

Sensitivity

As suggested by Wever & Lawrence (1954), and Wever (1959 1960), the sensitivity of the CM responses in man was expressed as the sound pressure level (dB SPL) necessary to produce an arbitrary voltage of CM response, measured in the linear portion of the intensity function of the CM Throughout this experiment the peak to peak amplitude of the summed CM responses displayed on the oscilloscope of the computer will be refered to as the amplitude or magnitude of the CM response. The sensitivity of the CM response was measured at levels of 0.1 microvolts, 0 3 microvolts and 1.0 microvolts, for frequencies of 500 Hz and 1000 Hz by both the extratympanic method and the intratympanic method. These results are listed in Table 1 in which the values (dB SPL) of the sensitivities represent the averages of 5 normal subjects together with the individual values for the intratym

bursts of pure tone differed in a great degree from that in response to the continuous pure tone. Figure 5 illustrates the time course and waveform of the summed response to the tone bursts. The pattern in Figure 5 involves an alternating current response which reproduces the sinusoidal waveform of the tone burst, as a main component of this complicated response Such an alternating current response repre sents *the CM response itself* Beside the CM response, the following changes in the waveform are observed 1) negative or positive shifts of the base line of the tracings, and 2) negative peaks or humps super imposed at the beginning of a train of sinusoidal (CM) waves. Such distortions in combination with the CM response modifies the precise reproduction of the trapezoidal *envelope of the tone burst as shown* in Figure 5 These waveforms of the responses to the pure tone bursts from human beings are in very close agreement with those reported for animals by several investigators (Goldstein 1954 Pestalozza & Davis, 1956 Davis 1958 1960 Davis et al 1958 a b Anggård 1965). The base line shift of the tracings suggests the SP The polarity of the base line shift varied with the individuals. No systematic relation of the SP in man to the stimulating factors has been observed with the intratympanic electrode. Such inconsistency in the polarity of the base line shift might be caused by considerable variations in placement of the intratympanic electrode on the promontory

Another important distortion is the negative peaks or humps, undoubtedly due to the admixture of the AP The negative peaks (AP) were often differentiated well from the otherwise sinusoidal wave of the CM at high frequencies above 1000 Hz. The appearance of the AP response in man to the pure tone bursts was compatible with the re sults in animals reported by Stevens & Davis (1938) and Davis (1957).

Figur 6 shows the combined responses of the CM with the AP to *the tone bursts from the human promontory* The proportion of the mixture of the AP and the CM varied with the frequency of the stimulus. The higher the frequency the more distinctly the AP could be distinguished from the CM It was not surprising that the magnitude of the AP varied with changes in the rise decay time of the tone burst. The summed responses to the short burst stimuli from the external acoustic meatus were a mixture of the CM and the AP with out the appearance of the SP The magnitude of the summed responses obtained by the extratympnic electrode was at least about 5 to 10 times less than that obtained by the intratympanic electrode Figure 7 illustrates differences in the waveforms of the complex responses between those two electrodes.

From these facts we have reached the working hypothesis that the extracochlear response in man to a short burst of pure tone was a complex response consisting of the CM *AP and SP in uncertain*

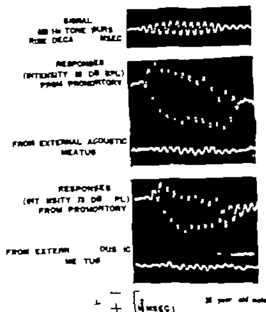


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TABLE I *CM sensitivity of the normal human ear as measured under two conditions (1) extratympanic recording from the external acoustic meatus and (2) intratympanic recording from the promontory*

Amplitude of CM in microvolts (peak to-peak)	Human CM sensitivity in dB SPL 500 Hz		1000 Hz	
	Meatus	Promontory	Meatus	Promontory
0.1	64 (55–74)	48 (40–59)	70 (64–77)	57 (50–61)
0.3	79 (71–86)	57 (49–69)	84 (79–97)	67 (59–77)
1.0	—	67 (58–80)	—	76 (68–82)

The sensitivity refers to the sound pressure level (dB SPL) at 500 Hz and 1000 Hz necessary to produce a constant potential (0.1 microvolt 0.3 microvolts, or 1.0 microvolts) of the CM (see Text). The results of five subjects were averaged for the promontory recording, and those of seven subjects were averaged for the meatal recording. The number in each column from the second one to the fourth represents the average of the sensitivity with individual values of minimum and maximum in parentheses. The number in the first column indicates the voltage of the CM.

panic recording and the averages of 7 normal subjects together with the individual values for the extratympanic recording. Sometimes the potential of 0.1 microvolts was not high enough for accurate measurements of the magnitude of the CM responses because the distortions due to background noise was overwhelming. Such was the case that the sensitivity of 0.1 microvolts was estimated by a method of the linear extrapolation (Wever 1959 1966 McGill 1959). After determining the intensity function of the CM as will be explained later in the section dealing with the intensity function the measurements were extended downward to a level of 0.1 microvolts by extrapolating from the linear portion of the intensity curve at high intensities.

Table 1 shows that the sensitivity varies not only with the position of the electrode but with the frequency of the stimulus. The intratympanic electrode, as might have been expected was more sensitive than the extratympanic one. The differences in the sensitivity of 0.1 microvolts between the two electrodes averages 16 dB for 500 Hz and averages 13 dB for 1000 Hz. Likewise the differences between them in the sensitivity of 0.3 microvolts averages 22 dB for 500 Hz and averages 17 dB for 1000 Hz. Overall the difference in the sensitivity between these electrodes on the average was about 20 dB. These differences represent the loss of the sensitivity caused by the extratympanic electrode.

Pseudo threshold

The lower limit of the potential at which the CM response became obscured by background noise was about 0 1 microvolts under favorable conditions of both the intratympanic electrode and the extratympanic electrode, using a summing or averaging number of 500 responses. Therefore, we chose the sensitivity of 0 1 microvolts as a measure of the lowest intensity that will produce a just detectable response from the trace on the oscilloscope, in preference to a conventional use of thresholds" or detection thresholds" The potential of the CM res ponses of 0 1 microvolts obtained from the subjects with normal hearing has fallen safely within a linear range of the intensity function as will be stated below The linear extrapolation (Wever 1959 1966) was applied to measurements of the sensitivity of 0 1 microvolts, as listed in Table I.

The visually detectable thresholds for the subjects with normal hearing ranged from about 40 dB SPL to about 60 dB SPL over fre quencies from 500 Hz to 1000 Hz in the intratympanic recordings and ranged from about 50 dB SPL to about 70 dB SPL over the same fre quencies in the extratympanic recordings. These results were in good agreement with those of the sensitivity of 0 1 microvolts. The sensiti vity of 0.1 microvolts may be compatible with a pseudo threshold" as designated by Davis 1957).

Strictly speaking, the CM is a continuous function of the intensity f the stimulus and does not have a threshold (Stevens & Davis, 1938 Da is, 1957 Wever 1959 1966). With regard to the measurement of the threshold for the CM Wever 1966 has laid much stress on the point that the detection threshold procedure has nothing to recommend it a d should be eliminated from future research in this field.

The pseudo threshold or the sensiti ity of a small response, how e er seemed to be useful in analyzing and describing the CM response in man recorded by means of a computer for purposes of objective audiometry

Intensity Functions

The mag itude or mplitude peak to peak) of the CM to continuous p re tones, but not to the sho t bursts of pure tone, was measured from the subjects with normal hearing as a function of the sound press re level of the stimulus intensity over a range from a low level ne s bjecti thresh lds to levels near 100 dB SPL, both by the e tratympanic method and by the intratympanic method. The frequency of the timulus ranged from 500 Hz to 1000 Hz. The magnitude was plotted n a logarithmic scale of the ordinate against the sound pressure le el f the abscissa. This is commonly known as the intensity function f the CM. A large literature has published on the intensity function

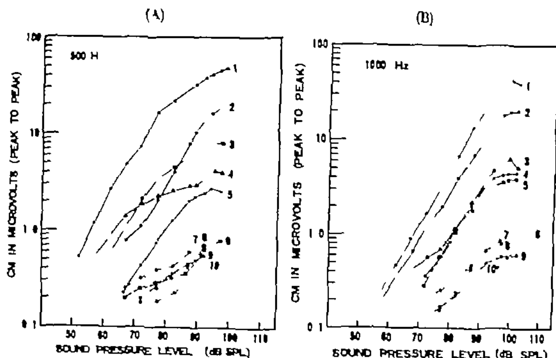


Figure 8. Intensity functions of the CM responses at 500 Hz (A) and 1000 Hz (B) in man. Amplitudes (peak-to-peak) of the CM responses, recorded with the intratympanic electrode (heavy lines) and the extratympanic electrode (broken lines), are represented as a function of the sound pressure level of the stimulus (dB SPL). The indicated number of each curve identifies the individual.

in animals (*cf.* Stevens & Davis 1938, Tasaki et al. 1952 a, b, 1954, Wever & Lawrence 1954, Davis 1951, 1957, 1958 a, b, Wever 1966), but few studies have been reported for human beings (Ronis, 1966, Ruben 1968).

Figure 8 shows intensity functions recorded both from the external acoustic meatus and from the promontory in man for two frequencies of 500 Hz and 1000 Hz. Figure 9 shows a set of intensity functions obtained from the external acoustic meatus over a range of frequencies from 500 Hz to 1000 Hz.

1) Form of the intensity functions

The form of the intensity functions varied to a great extent with the *position of the electrode*. In general, a typical intensity function for responses from the promontory is nearly linear in relation with the sound pressure level of the pure tone until the intensity reaches some high level at which the curve departs from the linear relation (heavy lines in Figure 8 A, B). The slope of the curve in the double logarithmic coordinates is very close to *1.0 (unity)*. *The upper limit* of the linear relation ranges approximately from about 90 dB SPL to about 100 dB SPL.

Our findings on the input-output relation of the CM as recorded from the promontory are essentially similar to those previously reported

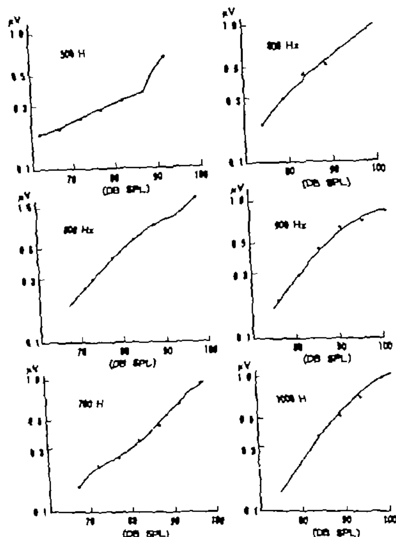


Figure 9. Intensity functions of the CM responses recorded from the external acoustic meatus ... man K. L. ... 19-year-old femal ... normal hearing). The frequency of the stimul ... 500 Hz, 600 Hz, 700 Hz, 800 H ... 900 Hz, and 1000 Hz. Ordinates: Amplitude peak to-peak of CM ... microvolts. Abscissae: Sound intensity in dB relati e to 0.0002 d ne cm

for the round window recordings in animals (*cf.* Stevens & Davis, 1938; Tasaki et al. 195_, a; Wever & Lawrence, 1954; Anggård, 1965; Shiraiwa, 1966). For the intratympanic recording, it seems reasonable to assume that when an electrode is placed in contact with the promontory it best records effectively from the hair cells near the basal end of the basal turn. This is mainly because the promontory is produced ... natomically by the bulging basal turn of the cochlea and the electrode at this site reflects the activity of the hair cells in its

A

B

SOUND PRESSURE LEVEL (dB SPL)

Figure 5. [illegible] at the CN [illegible] 500 Hz (A) and 2000 Hz (B) [illegible] at the CN [illegible] electrode [illegible] are represented as a function of the sound pressure level of the stimulus (dB SPL). The [illegible] number at each curve [illegible].

[illegible] & Davis [illegible]; [illegible] et al. [illegible]; Wever & Lawrence [illegible]; Davis [illegible]. [illegible] have been [illegible].

Figure [illegible] shows [illegible] 500 Hz and 2000 Hz. Figure [illegible] shows [illegible] from 500 Hz to [illegible].

[illegible]

The [illegible]

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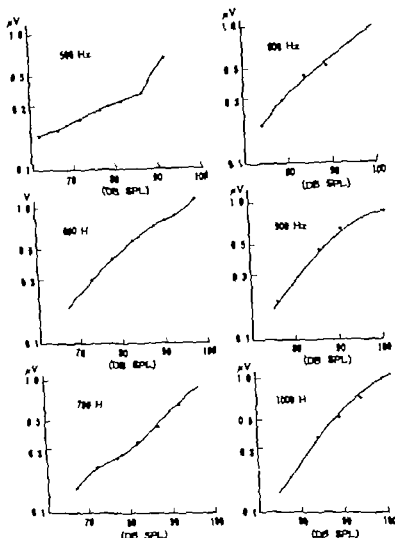


Figure 9. Intensity functions of the CM responses recorded from the external acoustic meatus ... K. I. ... 19-year-old female, normal hearing. The frequency of the stimulus: 500 Hz, 600 Hz, 700 Hz, 800 Hz, 900 Hz, and 1000 Hz. Ordinates: Amplitude peak-to-peak of CM ... microvolts. Abscissae: Sound intensity ... dB relative to 0.0002 dyne cm.

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immediate vicinity

On the other hand intensity functions for responses as recorded from the external acoustic meatus are not quite linear even at their lower ends (broken lines in Figure 8 A B and Figure 9). The slopes of the curves in the double logarithmic coordinates are significantly less than 1 0 The nonlinear relation to the stimulating intensity holds in general at frequencies of 500 Hz and 1000 Hz over a range of intensity from about 60 dB SPL to 100 dB SPL. This is a very important difference between the intratympanic and the extratympanic recordings. What the difference means appears to be more than a simple displacement of the curves to the right on the intensity axis such as might be expected from greater attenuation at the more remote electrode.

Such a nonlinear relation of the CM response as recorded from the external acoustic meatus may be explained as due to the remote position of the recording electrode and its different orientation with respect to the anatomical source of the generator potentials (the CM). Namely for the extratympanic recording an electrode is not applied to the cochlea directly but to the osseous portion of the meatus at a certain distance from the whole cochlea. The electrode in the meatus may record more effectively from more apical response areas in the basilar membrane involving the peak regions of the mechanical displacement than when the electrode is on the promontry Consequently the response may represent the activity of all the hair cells which are operating nonlinearly in the more apical regions of the cochlea.

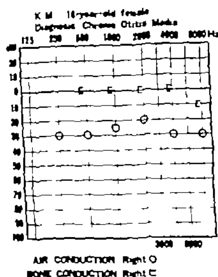
These observations lead to the conclusion that a general trend toward the linearity is observed from the intensity function for the intratympanic recording whereas the nonlinearity is common in the curves for responses recorded by the extratympanic electrode

2) *Nonlinearity and the maximum of the CM*

Accurate measurement of the upper limit of the linear relation was impossible in this experiment because of the irregularities in the intensity functions The estimated potentials of the levels at which the nonlinearity appeared in the intensity functions were ranged from approximately 2 microvolts to 40 microvolts for intra tympanic recording and from 0 5 microvolts to 1 0 microvolts for extratympanic recording The intensities corresponding to such potentials were approximately 80 dB SPL to 95 dB SPL

The intensity functions for intratympanic recording in the subjects with normal hearing tend to be nonlinear and asymptotic at intensities of more than about 90 dB SPL. Although the increase of the intensity function was less rapid (nonlinear) at these high intensities in comparison with the linear increase at low intensities all the curves except for a few cases did not attain a maximum of the CM at intensities up

(A) (B)



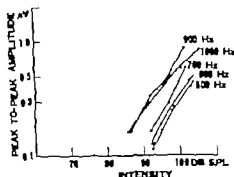


Figure 10. Intensity functions of the CM responses a patient with conduct ve deafness chronic otitis media. Otology findings: The ossicula chain was not disrupted. The eardrum was scarred and retracted with posterior perforation nd suggesting the adhesions (A) Audiogram. The audiometer which had the reference level of zero dB on the basis of the Japanese Industrial Standard (JIS) was used throughout this investiga tion. The JIS reference lev l pproximated t the ISO-1963 reference lev l. (B) Intensity functions at 800 Hz, 600 Hz, 700 Hz and 1000 Hz, measured with the extratympanic lectrode from the external acoustic meatus, as function of the sound pressure le l.

to 100 dB SPL. These exceptional cases formed a horizontal plateau or a peak of the intensity function at an intensity of about 100 dB SPL. No attempt to determine the maximum of the CM was made in the present tudy Gross estimation was tried simply by e trapolating the curve upwards along its asymptotic course The estimated potential of the maximum of the CM ranged from 5 micro olts to 50 microvolts for intratympanic recording, and from 0 6 microvolts to 1 5 microvolts for extratympanic recording. No systematic relation of the maximum of the CM to the frequency of the stimulus was found The intensity at which the maximum of the CM would be attained appeared always to be more than 100 dB SPL.

The CM Responses in Conductive Deafness

All the patients with conductive deafness were examined by the extratympanic method alone in this experiment. Efforts have been mad t compare the intensity functions obtained from the patients whose hearing losses were more than 30 dB for frequencies of 500 Hz and 1000 H with those obtained from the normal subjects.

In general the form of the intensity function in conductive deaf

ness scarcely differed from that in normal hearing except that the former shifted to the right on the abscissa. The results may be summarized by saying that the sensitivity of the CM in conductive deafness relates to the degree of hearing loss in the audiogram. The more the hearing loss increased the higher the intensity was required to produce the same level of the CM as obtained from the subjects with normal hearing Quantitative correlation however between the sensitivity of the CM and the hearing loss of conductive deafness has not been settled in this study

In conclusion an interesting example of the intensity function for a patient with chronic otitis media is illustrated in Figure 10 in which the slope of the input output functions is nearly 1 0 (unity), although the response is recorded from the external acoustic meatus. The reasonable interpretation may be that the electrical conducting pathways to the electrode have been modified by the middle ear adhesions or secretion of fluid in the middle ear In the case of inflammation of the middle ear it has to be borne in mind that the conditions of electrical conduction in the tympanic cavity may vary greatly from those of the normal ears

The CM Responses in Sensorineural Deafness

1) The intensity functions

Under such heading subjects were selected out of a number of patients who have suffered from sensorineural deafness diagnosed as cochlear origin by tests such as pure tone audiometry speech audiometry Bekesy audiometry recruitment tests, and so on The CM responses to the continuous pure tones with frequencies of 500 Hz, 600 Hz, 700 Hz 800 Hz 900 Hz, and 1000 Hz, were recorded both from the external acoustic meatus and from the promontory in these patients. The highest intensity of the pure tone stimuli was limited to a level of 100 dB SPL or slightly above

Although great effort was made to determine the intensity function from all patients, a number of the patients with hearing reduced by more than 80 dB hardly responded at all even to the highest intensity of the stimulus. A few examples will show that the intensity function could not be measured

Figure 11 is an example of no response to pure tone stimuli of 500 Hz and 1000 Hz, which was obtained from a patient who suffered from unilateral sudden deafness on the left side with a severe hearing loss of as much as 80 dB to 90 dB In contrast he had normal hearing for the right ear with typical form of the intensity function

Figure 12 displays another example a patient had long suffered from progressive bilateral sensorineural deafness. His audiogram showed a total hearing loss in the right ear and a residual hearing of 80 dB

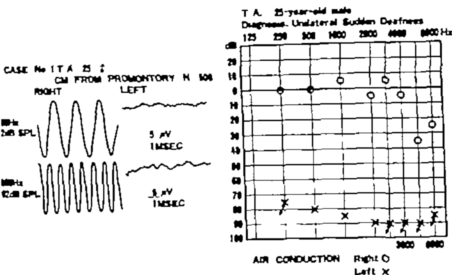


Figure 11. The CM response recorded from the promontory of a patient with unilateral sudden deafness, showing no response in the affected ear.

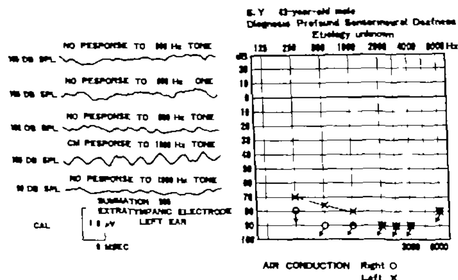


Figure 12. Residual CM response recorded from the external acoustic meatus of patient with bilateral severe sensorineural deafness. It is noticed that residual hearing over range of frequencies from 250 Hz to 1000 Hz is seen in his audiogram. All the summed waveforms were recorded from the left ear.

HL to 90 dB HL for frequencies of 500 Hz and 1000 Hz in the left ear. No response was recorded from the right ear for the two frequencies. The left ear responded very slightly to the 1000 Hz tone at the intensity of 100 dB SPL. Such slight a response may be called a

residual CM response" on the analogy of a residual hearing in a pure tone audiogram The residual response indicates the sensitivity (pseudo threshold) in this case of a severe hearing loss. But it was too small to plot the intensity function with any accuracy

2) Patterns of the intensity function

We are far from offering a detailed explannation of the quantitative correlation between the audiologic pattern and changes in the intensity function Therefore at the present time we merely classify various forms of the intensity functions

One of the most intriguing forms was the same pattern as the intensity function obtained from subjects with normal hearing This seemed to be associated with relatively slight hearing losses. Another was an abnormal pattern which was readily differentiated from the normal pattern by the following differences 1) overall reduction in potentials of the CM 2) distorted nonlinear form of the intensity function and 3) overall shift of the intensity function to the right on the intensity axis. These changes are illustrated in the next section Yet another was an incomplete pattern which seemed to be a transitional form from the normal pattern to the abnormal pattern suggesting an early stage of abnormality

The patterns of the intensity function in sensorineural deafness can be grouped in two categories 1) the normal pattern and 2) the abnormal pattern with no linear segment Almost all the patients with a moderate or severe hearing loss exhibited the abnormal pattern as might have been expected However the evidence was insufficient to define the quantitative change in the intensity function in sensorineural deafness any more positively

3) Clinical cases

Four cases with sensorineural hearing loss serve as examples.

Case 1 a 20 year old female with streptomycin deafness, shown in Figure 13 showed a rapidly increasing hearing loss for frequencies above 4000 Hz, associated with normal hearing for all other frequencies. For all the frequencies except 1000 Hz the intensity functions measured by the extratympanic method showed the normal pattern At 1000 Hz the intensity function was shifted slightly to the right and the curve had a nonlinear relation to the sound pressure level The sensitivity of 0 3 microvolts was 80 dB SPL for a 1000 Hz tone and 75 dB SPL for all other tones. The potential of the CM response to the stimulus intensity of 100 dB SPL ranged from 0 7 microvolts to 0 6 microvolts for all frequencies. In summary the intensity function for 1000 Hz showed an incomplete form of the abnormal pattern but the others showed the normal pattern

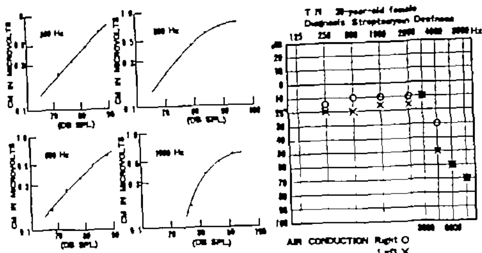


Figure 13. Audiogram and intensity functions of the CM responses of patient (case 1) with streptomycel deafness. Each of the intensity functions was measured from the left ear, using the xtratympanic lectrode.

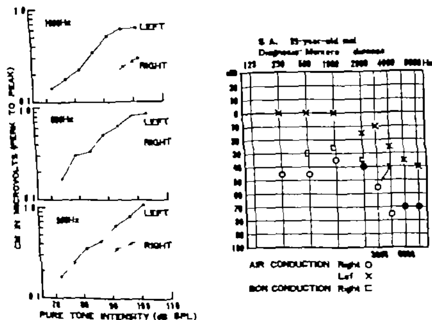


Figure 14. Intensity functions of the CM responses I patient (case 2) with Ménière and hi audiogram. Each of the ntensity functions was measured both from the left ear and from the right ear simultaneously using lectrodes placed pproximately at the same positions i the external acoustic meatus.

Case .. a 39 year old male with an unilateral hearing loss of the pin cochlear type in the left ear caused by Ménière's disease, was examined by the extratympanic method. An audiogram (Figure 14)

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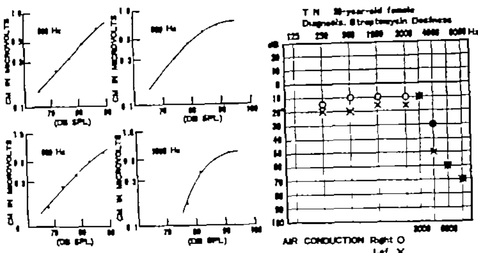


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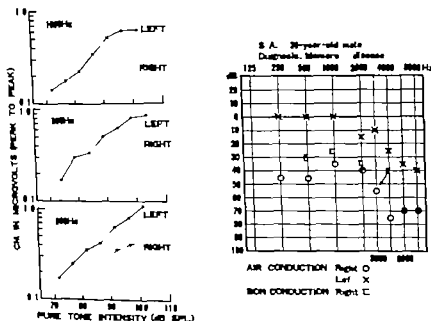


Figure 14. Intensity functions of the CM responses in a patient (case 2) with Ménière's disease and his audiogram. Each of the intensity functions was measured both from the left ear and from the right ear simultaneously using electrodes placed approximately at the same positions in the external acoustic meatus.

Case 2, a 39 year old male with an unilateral hearing loss of the pan cochlear type in the left ear caused by Ménière's disease, was examined by the extratympanic method. An audiogram (Figure 14)

shows a moderate flat hearing loss in the low and middle frequencies, associated with a steep fall of hearing loss in the high frequencies above 4000 Hz. The binaural loudness balance test at frequencies of 500 Hz and 1000 Hz gave complete recruitment in the right ear Bekesy tracings were of small amplitude for a continuous pure tone stimulus in the affected ear The CM responses were recorded from both ears under the same experimental conditions.

Figure 14 illustrates that for all frequencies the intensity functions in the right ear shift about 20 dB towards the right on the intensity axis parallel to those in the left ear Thus the right ear was about 20 dB less sensitive than the left ear Another interesting point was that there was no evidence for a rapid slope of the intensity function obtained from the ear with recruitment at frequencies of 1000 Hz and 500 Hz. Both the intensity functions measured from the normal ear and from the affected ear with recruitment were nearly parallel to each other This is a very interesting point in addition to which the amplitude of the response recorded from the affected ear is not reduced for the reduced sensitivity shown by the audiogram

On the other hand there were some exceptions in which the slope of the straight portion of the input output curve in the affected ear with recruitment was significantly less than unity Such observations were not compatible with those shown in Figure 14 More experimental work is necessary for a conclusive explanation of the input output functions obtained from the ear with recruitment.

Case 3 a 20 year old female with a bilateral downward sloping hearing loss caused by progressive sensorineural deafness with unknown etiology was examined by the intratympanic method As shown in Figure 15 a distinctive feature of the audiologic pattern was a severe hearing loss of more than 70 dB in the high frequencies above 2000 Hz. The intensity function could be measured only at 500 Hz, because of no response to the stimulus with higher frequencies above 600 Hz. The intensity function at 500 Hz is nonlinear and it attains a maximum at 0 9 microvolts. The value of 0 9 microvolts was significantly lower than the maximum obtained from the normal subjects (5 micro volts to 50 microvolts). The slope of the straight portion of the curve is significantly less than unity These observations indicate that the input output relation of case 3 is the abnormal pattern with no linear segment.

Case 4 a 65 year old male with a bilateral flat hearing loss in presbycusis as shown in Figure 16 was examined by the intratympanic method The intensity function could be obtained only at 1000 Hz. The curve in Figure 16 rises at first linearly and soon it becomes flat The curve reaches its maximum at about 100 dB SPL. The maximum voltage is 0 4 microvolts. The sensitivity of 0 1 microvolts is about

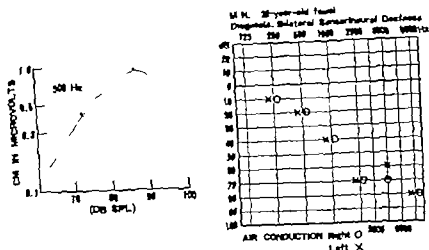


Figure 15. Intensity function of the CM response at 500 Hz in patient (case 3) with bilateral progressive sensorineural deafness, and his audiogram. No response to the pure tones t 600 Hz, 700 Hz, 800 Hz, 900 Hz, and 1000 Hz, was noticed. The electrode was placed on the promontory in the left ear

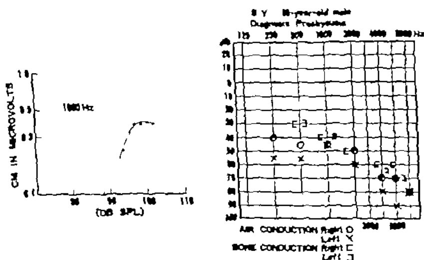


Figure 16. Intensity function of the CM response t 1000 H in a patient (case 4) with presbycusis, and his audiogram. The intensity function was measured from the promontory in the right ear. No response to the pure tones at 500 Hz, 600 Hz, 700 Hz, 800 Hz, and 900 Hz, could be recorded from this subject.

90 dB SPL, which is 30 dB less sensitive than the normal value. A residual CM response to the 500 Hz tone with an intensity of 100 dB SPL was recorded. No response to 800 Hz tone was recorded The slope of the straight portion of the curve at 1000 Hz is about 1 0. These findings on the intensity functions in case 4 seemed to be quite

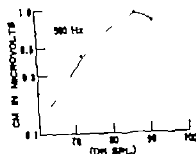
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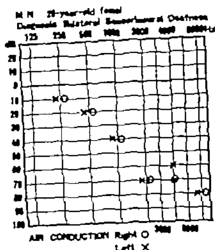
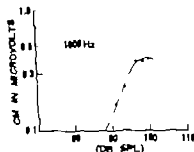


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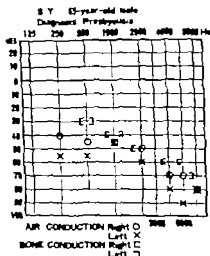


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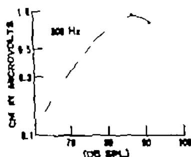
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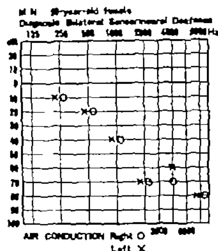
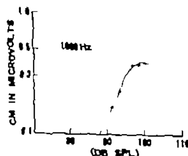


Figure 15. Intensity function of the CM response at 500 Hz in a patient (case 3) with bilateral progressive sensorineural deafness, and his audiogram. No response to the pure tones t 600 Hz, 700 Hz, 800 Hz, 900 Hz, and 1000 Hz, was noticed. The electrode was placed on the promontory in the left ear.



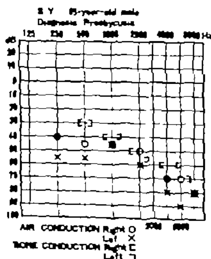


Figure 16. Intensity function of the CM respones at 1000 H in patient (case 4) with presbycusis, and his audiogram. The intensity function was measured from the promontory in the right ear No response to the pure tones t 500 Hz, 600 Hz, 700 Hz, 800 Hz, and 900 Hz, could be recorded from this subject.

90 dB SPL, which is 30 dB less sensitive than the normal value. A residual CM response to the 500 Hz tone with an intensity of 100 dB SPL was recorded No response to 800 Hz tone was recorded. The slope of the straight portion of the curve at 1000 Hz is about 1.0 These findings on the intensity functions in case 4 seemed to be quite

contradictory to those on case 2 and case 3 In case 4 changes in the intensity function was greater at the low frequency (500 Hz) than at the high frequency (1000 Hz), whereas in case 2 and case 3 the changes were more remarkable for the 1000 Hz tone than for the 500 Hz tone. Such differences in the CM responses between them are very probably due to differences in etiology and pathology of these cases of sensori neural deafness.

Before closing this section it should be pointed out that unfortunately the CM response for the frequency range from 2000 Hz to 8000 Hz could not be recorded throughout this entire experiment because the frequency range of the computer was limited to a low frequency range from 0 Hz to 1500 Hz. It will be essential to include in our future study a more detailed analysis of the CM in man for the higher frequencies

DISCUSSION

Extracochlear electrodes as used in this study are entirely favorable for recording human cochlear responses because they are simple and the cochlea is completely uninjured Davis (1957), however pointed out that extracochlear electrodes were in general quite inadequate for analysing intracochlear events because they recorded a mixture of AP CM and SP and also a mixture of responses from various parts of the cochlea Despite these serious limitations, the use of extracochlear electrodes is indispensably necessary for non surgical recording of the human cochlear potentials. As we have already seen there are important differences between the intratympanic and extratympanic methods for non surgical recording of the CM with respect to the pattern of the input output function Namely the recording electrode on the promontory tends to give the linear input output relation with a slope of unity whereas the electrode in the external acoustic meatus produces the nonlinear relation with a slope of significantly less than unity We may expect from these results that the hair cells near the basal end of the basal turn of the cochlear will contribute most readily to the potential seen at the promontory On the contrary the external acoustic meatus may be the more favorable position of an electrode for recording effectively the contributions of the more apical hair cells in the broader regions of the basilar membrane than does the electrode on the promontory In any event further studies into the question as to how much changes in various parts of the organ of Corti are recorded with these extracochlear electrodes are necessary

Usually in the measurements of human cochlear potentials, effects of the physiological activities comming from other tissues and organs than the cochlea in the subject himself upon the response must be

taken into account. There are a number of possible causes of such distorting factors which may mask and distort the simple input output relation of the CM to the sound pressure level (*cf* Stevens & Davis, 1938 Wever & Lawrence, 1954 Hepp Reymond & Palin 1968). Among them actually three distorting factors may be commented on for human subjects 1) physiological noise comming from the subject himself 2) reflex contractions of the middle ear muscles, and 3) the combination of the cochlear nerve action potential responses. The effects of all these factors on the simple input output relation of the CM may vary of course, with the intensity of the stimulus, with the frequency of the stimulus, with the condition of the subject, and with the position of the electrode. Theoretically they are not to be confused with the deviation from linearity due to arrival at limits of intensity in the generation of electrical potentials (CM) in the individual hair cells (Stevens & Davis, 1938). Practically however it must be difficult in human experimentation to differentiate clearly the effect of one dis torting facotor from another

Extensive cotributions to clinical studies on the human cochlear potentials have been made by Ruben and his colleagues (1959 1960 1961 1962, 1964, 1966, 1967). A method of graphic representation called the cochleogram (the sensitivity curve) has been developed by them. Ronis (1966) attempted to compare the intensity functions for responses recorded under preoperative conditions in otosclerosis with those recorded under the postoperative conditions. He observed a general increase in the CM output for all frequencies after stapedectomy Furthermore, Ruben (1967) studied various changes in pattern *of the* intensity functions for patients with various hearing losses. These observations are at least partially in good agreement with our results.

In electrophysiological studies of cochlear lesions in animals, many investigators have observed at least *two changes* in the input output relations of the CM to the stimulus intensity 1) a *parallel shift* of the linear portion of the intensity function to the right side and 2) reduction in the maximum CM voltage (*cf* Davis *et al*, 1953 Wever & Lawrence, 1954 Davis, 1957 Eldredge et al, 1957 1958 1959 Lawrence et al 1959 Simmons & Beatty 1962 Wever 1966 Elliott, 1967 Ogawa 1968). It seems too early *to say how* suitable to the case of human beings these criteria in animals will prove Clinical sig nificance of the intensity f nction in sensorineural deafness would be a real puzzle in objective audiometry and would probably take much time to be resolved.

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ZUSAMMENFASSUNG

Zur Registrierung der Cochlearmicrophonics (CM)-Antworten beim Menschen wurde eine nichtchirurgische Methode entwickelt bei der Neue aktive Elektroden in Kombination mit einem Mittelwertrechner verwendt werden. Die eine der Elektroden war als Nadel gestaltet und wird im äusseren Gehorgang placiert, die andere besteht aus einem rostfreien 80 micron dünnen Stahldraht und ist versehen mit einer speziellen Kanüle am Promontorium oder in der Rundfensternische gelegen Das Anbringen der Elektroden ist für den Probanden schmerzlos und gelingt ohne Blutung Als akustische Reize benutzt der Verf reine Dauertöne und kurze Tonimpulse als Versuchspersonen normalhörende Freiwillige sowie Patienten mit Schalleitungs und Innenohrschwerhörigkeit Alle Untersuchungen fanden in einem schalldichten Raum statt Die Resultate sind in folgender Weise zusammenzufassen

1 *Die normalhörenden Versuchspersonen zeigten regelmässig und beständig* CM Antworten sowohl am äusseren Gehörgang als am Promontorium.

2. Bei Verwendumo von Tonimpulsen wurden am Promontorium CM Summenaktionspotential (AP)- und Summationspotential (SP) Antworrten registriert und am äusseren Gehörgang CM und AP Antworten.

3. Bei Verwendung von reinen Dauertönen waren die CM sowohl am äusseren Gehörgang wie auch am Promontorium registrierbar

4. Die Form der Intensitätsfunktion am Promontorium stimmte bei normal hörenden Versuchspersonen vollkommen mit dem überein was von Elektroden messungen am runden Fenster bei Tieren bekannt ist

5. Einige der Intensitätsfunktionen von Patienten mit *Innenohrschwerhörigkeit* zeigten folgende abnorme Muster

(a) eine Verringerung der CM Grösse,

(b) eine Verzerrung *(nichtlineare Beziehungen),*

(c) eine parallele Verschiebung zur rechten Seite der Intensitätsfunktion hin.

6 Die Emphfindlichkeit der CM scheint in Beziehung zu stehen zum Grad des Hörverlustes im Audiogramm

7 Die nichtchirurgische Methode ist hinreichend praktikabel in der klinischen Routineaudiometrie zur Differentialdiagnose der Innenohrschwerhörigkeit.

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CLINICAL USE OF COCHLEAR NERVE ACTION POTENTIAL RESPONSES IN MAN FOR DIFFERENTIAL DIAGNOSIS OF HEARING LOSSES

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The whole-nerve action potential response (AP) of the cochlear nerve in man was stably recorded either from the external acoustic meatus or from the promontory by a non surgical method, using an average response computer. Acoustic stimuli were either clicks or tone pips. Subjects were 8 normal volunteers, 15 patients with sensorineural deafness, and 2 patients with conductive deafness. Both the intensity function of the latency of N and of the amplitude of N were measured from all the subjects. There were many variations in pattern of these curves that might be produced by conductive or sensorineural hearing loss. On the basis of the working hypothesis of a double organization, these results were interpreted.

The general conclusions are as follows:

(1) For normal hearing, the input-output function of N included the two distinct segments, the L curve and the H-curve, independent of the position of the electrode. Each of the segments might be generated by a different population of neurons and stimulated by a different class of sensory cells.

(2) For conductive hearing loss, the change in the latency and the amplitude seemed to be proportional to the degree of the hearing loss.

(3) For sensorineural deafness, three points may have clinical significance: (a) the overall reduction in amplitude of N_1, (b) the monotonicaly increasing form of the input-output function of N_1, in other words, the disappearance of the L-curve from the input-output relation, and (c) the prolonged latency of N.

(4) Our findings on the AP in man seemed to be practically identical with those reported for guinea pigs and cats.

INTRODUCTION

Recently a clinical method for non surgical recording of the human cochlear responses to acoustic stimuli has been developed in several laboratories independently by means of an average response computer (Yoshie et al. 1967, Yoshie, 1968, Portmann et al. 1967, 1968, Sohmer & Feinmesser 1967, Spreng & Keidel, 1968). The whole-nerve action potential response (AP) of the cochlear nerve in man has been recorded widely both from the external acoustic meatus and from the promontory with relative ease by the non surgical method. This is strong evidence

(dB SPL) of a 4000 Hz pure tone (for clicks) or a 4800 Hz pure tone (for tone pips) whose peak amplitude was the same the maximum amplitude of the clicks or the tone pips (*cf* Deatherage & Hirsh 1959 a Teas et al, 1962).

The subject lay on his back on a bed in an electrically shielded sound proof room equipped with an air conditioning system.

Electrodes were placed either on the external acoustic meatus or on the promontory in combination with a reference electrode on the earlobe. The electrode placement was performed under local infiltration anesthesia in the posterior wall of the meatus. Electrodes fixed to the human body remained quite stable over long periods of time during the examination

Responses to 500 successive clicks or tone pips were averaged or summed on line by an average response computer SAN'EI MEDIAC 401, with an analysis time of 31 25 msec. The summed waveform of the response was directly photographed on the face of an oscilloscope.

RESULTS

Normal Pattern of the AP in Man

Figure 1 is an example of the summed waveform of the AP recorded from the external acoustic meatus of a normal subject. The overall waveform is a series of peaks electrically negative with respect to the earlobe. This was quite the same as that recorded from the promontory near the round window In addition, the form is essentially identical with those reported for animals and human beings (*cf* Derbyshire & Davis 1935 Stevens & Davis, 1938 Teas *et al* 1962 Ruben et al 1960 Ronis, 1966).

The first and largest peak called "N_1 is followed by the secondary small peaks, called "N_2" and N_3" Usually these peaks are monophasic. They are separated by intervals of about 1 msec. Frequently the N_1 showed a diphasic wave, in which a large negative peak (N_1) was followed by a small positive deflection. The N_1 is the main component of the AP and the others are secondary components. The observations reported in this study are made on N_1

The latency of N_1 was measured from the instant of arrival of the click at the eardrum to the peak of N_1 as shown in Figure 1. The time of its arrival was determined by placing a condenser microphone at 33 cm distance from the driver unit.

Figure is the latency of N_1 recorded from the meatus as a function of click intensity The averaged latency for 5 normal subjects is plotted against the peak equivalent sound pressure level of the stimulating clicks. The latency decreases nonlinearly with the increase of intensity The upper and lower limits of distribution for sampling

to indicate that the AP as obtained from an extracochlear electrode placed somewhere remote from the round window may be applicable to a routine test for objective measurements of the overall functions in the cochlear nerve and the organ of Corti. As have been reported by Ruben and his colleagues (1960 1961 1963 1964 1966 1967), it would be impossible to record consistently the AP at some distance remote from the round window membrane in man without using the computer techinique for averaging or summation

In an earlier paper (Yoshie 1968), of particular interest might be the quantitative relationships between a few parameters of the AP in man and an intensity of stimulating clicks (1) the peak latency of N_1 was a very stable and consistent function of the sensation level of the click intensity and (2) the input output function of the peak to peak amplitude of N_1 includes two distinct segments or humps that are conveniently termed the L curve and the H curve respectively The present study extends these observations to patients with sensorineural deafness and conductive deafness for practical purposes of clinical use. Consequently an attempt was made to record the AP in patients with hearing loss, either from the external acoustic meatus or from the promontory and then to measure both the latency of N_1 and its amplitude as functions of click intensity

METHODS

A total of 25 subjects consisting of 8 with normal hearing 15 with sensorineural deafness, and 2 with conductive deafness, were employed in this study For each of the subjects both audiologic and otoscopic examinations were carefully carried out in advance.

The technique and the apparatus used in this study were the same as described fully in the article dealing with the human CM response in this special issue (1969) or in earlier papers (1967 1968), except for the following minor modifications of acoustic stimuli. Therefor only a brief outline need to be given of the experimental method

Acoustic stimuli were either clicks or tone pips of 4800 Hz given at an interval of 160 msec by a driver unit which was placed 30 cm lateral to the ear tested The electro acoustic transducer was completely shielded to avoid electrical artifacts on the records. Clicks were generated by applying a rectangular pulse of 0 1 msec duration to an audio amplifier Tone pips of 4800 Hz were made by passing a rectangular pulse of short duration through a band pass filter which was set to the same cutoff frequency (4800 Hz) both for high and low pass (cf Davis et al 1951).

The intensity of the clicks and the tone pips was measured as the peak equivalent sound pressure level that is, the sound pressure level

individual values of the latency are shown by dashed lines in Figure 2. It is noticed that there are surprisingly small individual variations in latency. Such consistency of the latency has already been reported for cats by Ruben et al (1962). The intensity function of N_1 as obtained from the promontory was a perfect duplication of the Figure 2.

As regards the AP in normal hearing, we can safely say that the latency of N_1 depends not on the electrode position or the individual differences of subjects but on the intensity of the stimulus.

As illustrated in Figure 1 the amplitude of N_1 is defined as the height from the base line of the tracing to the peak of N_1. The average for 5 measurements of the amplitude of N_1 at the same intensity of clicks was obtained for each of the 8 normal subjects. The averaged amplitude was used as data to be discussed. The responses were recorded at the following positions: (1) the promontory near the round window niche, (2) the promontory at some distance from the round window (3) the posterior wall of the meatus, 1 mm to 2 mm lateral to the annulus tympanicus, (4) the posterior wall of the meatus, 15 mm lateral to the eardrum, and (5) the outer end of the meatus.

Figure 3 is a set of input output functions of N_1 recorded at these various electrode positions as a function of the peak equivalent sound pressure level of the stimulating clicks. The amplitude in microvolts is plotted on a double logarithmic scale. The important point is that the input output curves are actually all similar in shape but differ chiefly by a factor of proportionality due to differences in attenuation at the different positions of recording. They also are practically similar to those reported for guinea pigs and cats (Rosenblith, 1959 Frishkopf & Rosenblith, 1958 Davis et al, 1958; Davis, 1960 1961 1962 Keidel, 1960 1964).

Generally speaking, as shown in Figure 3, the input output curve rises rapidly at first from a threshold level of *response* and then it continues to rise rapidly up to a knee or a top of the first hump The curve then rises along the second hump to the maximal level of output. The curve shows an inflection point at which the slope changes in the intensity region from 0 dB to 60 dB peak equivalent SPL. The names of the L curve and the H curve have been suggested to designate the two curves (Yoshie, 1968).

The amplitude of N_1 at the meatus near the annulus tympanicus is reduced to about one tenth of those recorded near the round window niche. Accurate measurements of the output of N_1 at the outer end of the meatus were difficult to make, because the response was con siderably attenuated, namely about one fifth of the output at the meatus near the annulus tympanicus.

Practically for the intratympanic recording from the promotory the electrode need not have been placed exactly on the round window

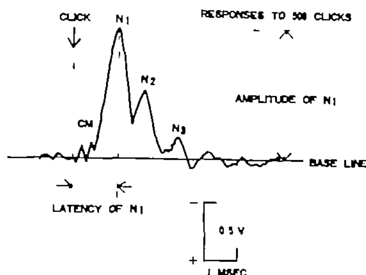


Figure 1. A typical summed waveform of the AP in man recorded at the external acoustic meatus by a non surgical technique. Responses to 500 clicks with an intensity of 100 dB peak equivalent SPL, given at an interval of 160 msec were summed by an average response computer with an analysis time of 31.25 msec. The subject was a [illegible]1 year old female with normal hearing. The vertical arrow in the upper left hand corner of the figure indicates the moment of arrival of the stimulating click. The base-line is an ideal line drawn simply by visual interpolation through the tracing of spontaneous activity to represent zero level of the amplitude of the response. In this and the rest of the figures upward deflection indicates negativity of the meatus (or the promontory) with respect to the reference electrode.

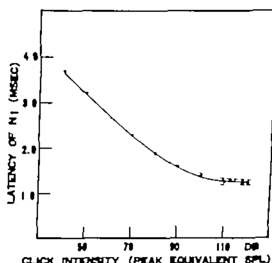


Figure 2. Latency of N1 in man recorded at the external acoustic meatus in relation to the intensity of the stimulating click. The ordinate is the latency in milliseconds, and the abscissa is the click intensity in dB peak equivalent sound pressure level (see Text). Each point on graph represents the arithmetic average of 5 normal subjects. Five measurements on latencies of N1 to the same intensity were made on each subject. Dashed lines indicate the extremely range of the individual latencies.

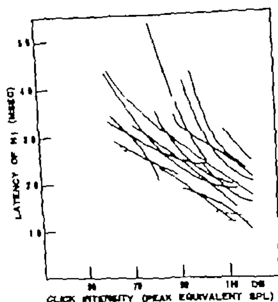


Figure 4. Latencies of N obtained from 15 patients with sensorineural deafness as a function of peak equivalent sound pressure level. Each curve (heavy line) is interpolated smoothly by eye through the verage of 3 measurements for responses to identical stimuli. An area surrounded by tw dashed lines indicated the normal range of the latency of N

is so stable that it will be useful for objective measurements of the hearing loss caused by pure conductive deafness.

(b) Sensorineural deafness

Figure 4 shows a group of intensity functions of the latency mea sured from 15 patients with sensorineural hearing loss, whose degree of loss varied to a great extent. There are many individual variations in latency but a general tendency for these curves to shift upwards and to the right to a varying e tent is exibited. Namely the latency of N_1 seems to be prolonged in comparison with the normal range of the latency But it may be too early to make a definite conclusion concerning the relation between the delay in latency of N_1 and the amount of hearing loss in sensorineutal deafness.

Some of the curves show an abnormally rapid rise of the slope which is inversely related to the click intensity Such remarkable delays seem to be characteristic of the latency in sensorineural deafness, because it has not been found in normal and conductive deafness.

Changes in amplitude

( ) Conductive deafness

The input output functions of N_1 were measured from the pro montory (Figure 5) and the external acoustic meatus (Figure 6). For conductive hearing loss, the input output curve shifted to the right on

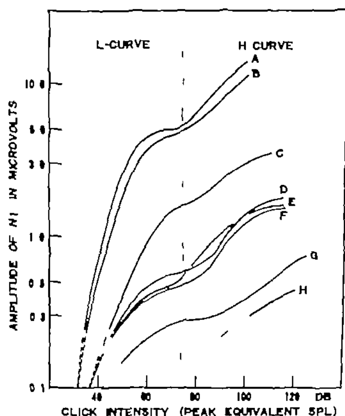


Figure 3. Input output functions of N_1 in man to clicks recorded at various positions of electrode placement. Amplitudes of N_1 are plotted on a double logarithmic scale against the peak equivalent sound pressure level. The eight curves are obtained from electrodes placed near the round window niche (A and B), on the promontory at some distance from the round window niche (C), at the external acoustic meatus near the annulus tympanicus (D, E, and F), on the meatus 15 cm from the eardrum (G), and at the outer end of the meatus (H). Each curve is drawn smoothly by visual interpolation, based on the average of 5 measurements for responses to identical stimuli in each subject. The subject has normal hearing. The letters attached to each curve designate different subjects. The vertical dashed line drawn in the center of the figure marks approximate separation between the L-curve and the H curve.

niche because the output of N_1 recorded by an electrode placed blindly somewhere on the promotory gave sufficiently accurate measurements. On the other hand, for the extratympanic recording, an active electrode should be placed near the annulus tympanicus.

Abnormal Patterns of the AP in Man

Changes in latency

(a) Conductive deafness

The intensity function of the latency for conductive loss was similar to that for normal hearing, except for a shift to the right along the intensity axis. The degree of the shift was proportional to the amount of heaing loss of the patients. A more extensive discussion of this problem is available in an earlier paper (1968). This simple relation

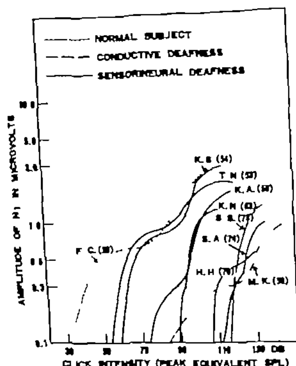


Figure 8. Variations in the input-output functions of N recorded from the external acoustic meatus of patients with various types of hearing loss. The parameter is designated as individual subject (letters) and as subjective threshold for click in decibels peak equi alent SPL (number in parentheses).

F. C. —with normal hearing. This curve represents typically two divisions of the input-output relation of N di ided by an inflection point at 70 dB peak equivalent SPL, the L-curve and the H-curve.

K. S. —with normal threshold, except for bilateral C-5 dip, due to acousti trauma. The form of the input-output function is the normal pattern. The L-curve is separated approximately from the H-curve by an nflection point t 85 dB peak equivalent SPL.

T. N. —with normal hearing, xcept for bilateral C-5 dip, with reduced threshold t 8000 Hz, due to streptomyci deafness. This curve is lmost the same as just described above.

K. A. —with moderate high tone loss, due t acoustic trauma. There is an inflection point at about 95 dB peak equivalent SPL, but the L-curve is diminished.

K. N. —with bilateral downward sloping audiogram, due to head trauma. The curve rises monotonicaly up to plateau. The L-curve is not seen.

S. S. —with gradual high tone loss, showing moderate to severe hearing loss, due to sensorineural deafness of unkno etiology. The curve is monotonicaly increasing function w th an abrupt slope.

S. A. —with unilateral flat udiogram with severe hearing loss, due to Ménière's disease. The curv rises abruptly in monotonic fashion up to maximal level.

H. H. —with severe sensorineural deafness, due to syphilis. The curv shows reduced amplitudes of N and monotonic rise.

M. K. —w th conducti hearing loss, due to chronic otitis media. The curve shows both the L-curv and the H-curve. It is displaced to the right along the intensity axis.

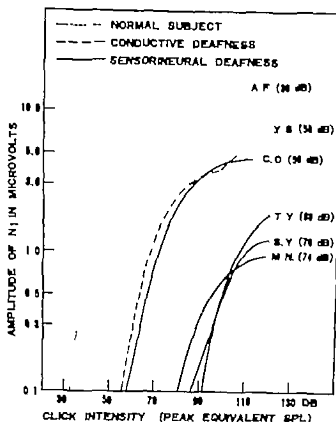


Figure 5. Variations in the input-output functions of N recorded from the promontory of patients with various types of hearing loss. The four curves represented by a heavy line obtained from patients with sensorineural deafness (C. O T Y S. Y and M. N). *The curve represented by a dashed line is obtained from a patient with pure conductive* hearing loss (Y S.). The dotted curve at the top represents a typical form of the input output function obtained from a normal subject (A. F). The numbers in parentheses indicate subjective thresholds for clicks in peak equivalent sound pressure levels. Each curve is interpolated smoothly by eye based on the average of 5 measurements for responses to identical stimuli

the intensity axis. The degree of the shift seemd to be proportional to the amount of hearing loss. Both the L curve and the H curve remained normal

(b) Sensorineural deafness

Both Figure 5 and Figure 6 illustrate typically various patterns of the input output functions in sensorineural deafness. All the curves were determined in response to clicks. These curves are represented by a smooth line rather than the actual data because this is the place to discuss a general trend of the input output functions in sensorineural deafness.

Figure 5 illustrates four cases with relatively severe hearing loss, and Figure 6 shows many cases including widely different degrees of hearing loss.

For sensorineural deafness, the typical form of the input output

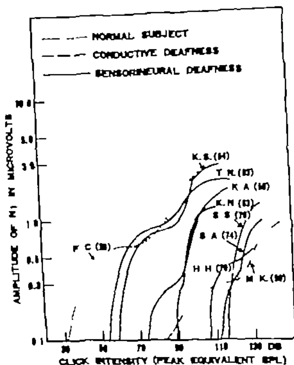


Figure 6. Variations in the input-output functions of N recorded from the external acoustic meatus of patients with various types of hearing loss. The parameter is designated as individual subject (letters) and as subjective threshold for click in decibels peak equivalent SPL (number in parentheses).

F. C. ——with normal hearing. This curve represents typically two divisions of the input-output relation of N divided by an inflection point at 70 dB peak equivalent SPL, the L-curve and the H-curve.

K. S. ——with normal threshold, except for bilateral C-5 dip, due to acoustic trauma. The form of the input-output function is the normal pattern. The L-curve is separated approximately from the H-curve by an inflection point at 85 dB peak equivalent SPL.

T. N. ——with normal hearing, except for bilateral C-5 dip, with reduced threshold at 8000 Hz, due to streptomycin deafness. This curve is almost the same as just described above.

K. A. ——with moderate high tone loss, due to acoustic trauma. There is an inflection point at about 95 dB peak equivalent SPL, but the L-curve is diminished.

K. N. ——with bilateral downward sloping audiogram, due to head trauma. The curve rises monotonically up to plateau. The L-curve is not seen.

S. S. ——with gradual high tone loss, showing moderate to severe hearing loss, due to sensorineural deafness of unknown etiology. The curve is monotonically increasing function with an abrupt slope.

S. A. ——with unilateral flat audiogram with severe hearing loss, due to Ménière disease. The curve rises abruptly in monotonous fashion up to maximal level.

H. H. ——with severe sensorineural deafness, due to syphilis. The curve shows reduced amplitudes of N_1 and monotonic rise.

M. K. ——with conductive hearing loss, due to chronic otitis media. The curve shows both the L-curve and the H-curve. It is displaced to the right along the intensity axis.

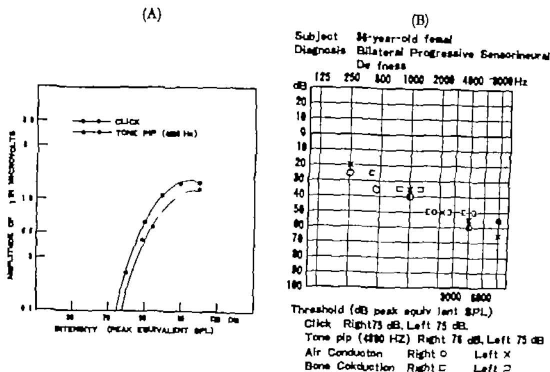


Figure 7 (A) Input output functions of N to clicks and tone pips of 4800 Hz recorded from the external acoustic meatus of a patient with bilateral progressive sensorineural deafness, and (B) the audiogram. Measurements were made on the left ear Both curves are monotonicaly increasing functions of the stimulus intensity The forms of these two curves are approximately the same.

curve (Figure 5) is a monotonicaly increasing function with a steep slope It rises very rapidly at first from the threshold response, and continues to rise sharply in a monotonic way up to a plateau or a maximal level of potential. Alternatively such a form may be explained as a disappearance of the L curve from the intensity function of N_1

Another important point is the reduction in amplitude of N_1 as demonstrated clearly in Figure 5. The amplitude of N_1 may be closely related to the amount of hearing loss at high frequencies above about 4000 Hz.

On the other hand there is a transitional form between the normal curve and the abnormal curve in Figure 5 Such a transitional pattern is shown in Figure 6 in comparison with both the typical pattern of normal hearing and the typical one of sensorineural hearing loss. For example, one of the curves, as labelled "T N " is almost the same as the normal pattern another curve labelled "K A. shows a tendency for the L curve to diminish

It appears well established for characteristic changes of the input output function in sensorineural deafness that (1) the reduction in amplitude of N_1 is significant and (2) the growth in amplitude of N_1 is rapid and monotonic as the click intensity is increased In other words the disappearance of the L curve may be characteristic of

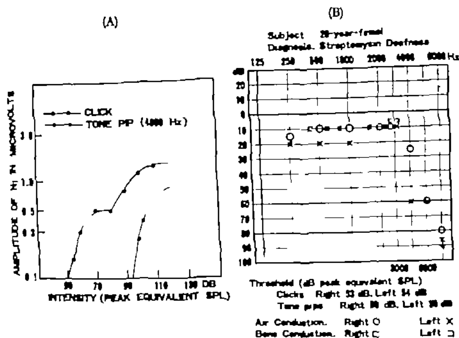


Figure 8. (A) Input-output functions of N to clicks and tone pips of 4800 Hz recorded from the xternal acoustic meatus of patient with streptomycin deafness, and (B) the audiogram. The curve for clicks represents both the L-curve and the H-curve, but that for tone pips shows the latter alone.

sensorineural deafness. As evidence in support of this view a few examples will suffice.

Figure 7 illustrates a case a 36 year old female with bilateral progressive sensorineural deafness of unknown etiology The AP was recorded at the meatus near the annulus tympanicus. The audiogram is a gradual high tone hearing loss. Both clicks and tone pips of 4800 Hz were used as acoustic stimuli.

The curves rise abruptly from a threshold response of 0 1 micro volts up to a maximal level of 1 5 microvolts. The dynamic range of these intensities were from 80 dB peak equivalent SPL to 110 dB peak equivalent SPL. The forms are typically monotonic. The curve for clicks is identical with that for tone pips of 4800 Hz.

Figure 8 illustrates a case, a 20 year-old female, with a bilateral abrupt high tone loss above 4000 Hz due to streptomycin deafness. The AP to clicks and tone pips of 4800 Hz was recorded at the meatus nea the annulus tympanicus. Click stimuli resulted in the normal pattern of the input output function, but tone pips produced only the H curve associated with the reduction in amplitude. Such difference between clicks and tone pips of 4800 Hz may be due to the differences in the time course and the frequency spectrum of these transient

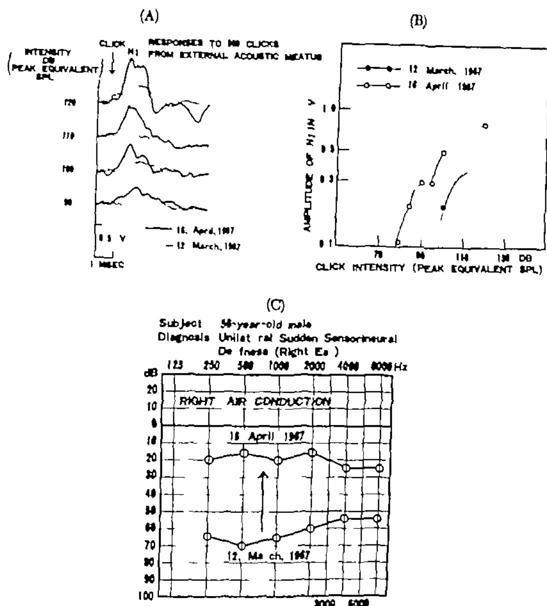


Figure 9. (A) Summed waveforms of the AP in sudden unilateral sensorineural deafness before and after treatment (B) Input output functions of N and (C) the audiogram.
(A) Responses to 500 clicks recorded at the external acoustic meatus were summed by a computer The waveforms represented by dotted lines show the AP recorded in the initial stage of sudden deafness (the most advanced stage of hearing loss). The waveforms drawn by heavy lines show the AP in the improved stage of hearing loss.
(B) Amplitudes of N are represented as a function of peak equivale t SPL of the stimu lating click. The amplitude in the initial stage of sudden deafness is greatly red ced.

signals (*cf* Stevens & Davis 1938 Deatherage et al 1959 b Davis 1961 Teas et al 1962). For this reason clicks may stimulate synchro nously a larger portion of the organ of Corti than the tone pips of 4800 Hz. For the tone pips, the motion of the basilar membrane may be confined to the basal turn

Figure 9 is a case a 56 year old male with unilateral sudden sensorineural deafness. The audiogram shows a great deal of improve

ment of hearing loss after treatment, amounting to about 50 dB In the initial stage with the most advanced hearing loss, the AP was remarkably reduced (Figure 9), and the input output curve is almost monotonic. In the improved stage with normal hearing the AP recovered fully and the curve represented both the L curve and the H curve.

DISCUSSION

The discussion will be centered upon the problem of the AP in sensorineural deafness. Three points may be commented on as essence of the criterion, for practical purposes, of the AP in man: (1) The marked delay in latency of N_1 (2) the marked reduction in amplitude of N_1 and (3) the monotonicaly increasing function of amplitude of N with a steep slope in relation to click intensities.

Significance of prolonged latency of N_1

According to Deatherage et al (1959b), and Davis (1961), the latency of N_1 may comprise both the neural delay originating from asynchrony of impulses (*cf* Tasaki & Davis, 1955 Davis, 1957), and the traveling wave delay due to the space time pattern of the traveling wave on the basilar membrane (*cf* v Békésy 1947). The neural delay seems to be the most important factor

It may be reasonable to presume that various types of damage or injury in the cochlea particularly in the organ of Corti may give rise to greater asynchrony of impulses. Consequently the higher the asynchrony the more the latency of N_1 may be prolonged.

Deatherage et al (1959 b) observed in guinea pigs that some interferences (masking, local fatigue and local injection of drugs) in the basal turn prolonged the latency of the AP response. They concluded that the latency of N_1 for clicks was increased whenever the neurons of the basal turn could not respond synchronously

Simmons and Beatty (1962) noticed in cats with acoustic trauma that many variations in latency of N_1 appeared in acoustic trauma. These observations on animals seem to be at least in part analogous to those on the human AP Some types of sensorineural deafness may be responsible for the abnormally prolonged delay of N_1

Significance of reduction in amplitude of N_1

The reduction in amplitude of N_1 may well be interpreted by the concept of the volley principle (*cf* Derbyshire & Davis, 1935 Stevens & Davis, 1938 Tasaki 1954 1957 Davis, 1957 1960 1961 Teas et al, 1960). According to them, the peak to peak amplitude of N_1 is fairly proportional to the number of fibers which are activated synchronously The f ct that the amplitude of N_1 in man was reduced

by the hearing loss due to sensorineural deafness may be in accord with the observations in guinea pigs by Pestalozza et al (1957), Eldredge et al (1958 1959), and Davis et al (1958).

Clinical use of the input output curve in man

As based on the widely held double organisation theory of the organ of Corti the two humps of the input output function for N_1 originate one from a small population with low threshold and the other from a larger one with high thresholds (Rosenblith 1954 a b Davis et al 1958 Davis 1960 1961 Keidel 1960 1964). Convincing evidence to support this hypothesis has been reported also for human beings (Yoshie 1968). The present results appear also to favor such a dual system of the sensory units in the periphery to the auditory pathway

There have been many extensive observations on the input output functions of N_1 measured from guinea pigs and cats with cochlear injuries from drugs acoustic trauma and venous obstruction (Davis et al 1958 Eldredge et al 1958 1959 Pestalozza et al 1957 Theissing 1963 Stange et al 1963 1964 1966 Keidel 1960 1964). These results in the animal experiments support the view that the appearance of the monotonic increase in amplitude of N_1 suggests a total or serious "subtractive loss" of the sensory units" belonging to the low threshold sensitive population (*cf* Davis, 1961 1962 Yoshie 1968). If we accept this, the same may be said of the changes in the AP in man for sensorineural deafness.

It is of considerable clinical significance that the abnormal pattern could be found in the intensity functions of N_1 for sensorineural deafness. The correlation between the audiologic pattern of the audiogram and the pattern of the AP has not been assessed at the present time but its study presents an intriguing field for differential diagnosis of cochlear lesions.

Many more clinical cases with sensorineural hearing loss should be examined by the non surgical method however befor a definite conclusion can be safely drawn about electrophysiological diagnosis for cochlear deafness and cochlear nerve deafness.

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ZUSAMMENFASSUNG

Das Summenpotential des Hörnerven beim Menschen (AP) wurde entweder vom äusseren Gehörgang oder vom Promontorium mit Hilfe einer nichtchirurgischen Methode und unter Verwendung eines Mittelwertrechners registriert. Als akustische Reize wurden Clicks und Tonimpulse verwendet. Als Probanden dienten 8 Normalhörende 15 Patienten mit Innenohrschwerhörigkeit und 2 Patienten mit Mittelohrschwerhörigkeit. Sowohl die Intensitätsfunktion der Latenz von N als auch die Ausgangsfunktion der Amplitude von N wurden bei allen Versuchspersonen gemessen. Es fanden sich viele Varianten im Muster dieser Kurven wahrscheinlich bedingt durch den Mittelohr bzw Innenohr Hörverlust. Diese Resultate werden auf dem Boden der Duplizitätstheorie diskutiert.

Zusammenfassend ergab sich

1. Für Normalhörende sich die Eingangs Ausgangsfunktion von N einschliesslich der L kurve und der H Kurve unabhängig von der Lage der Electrode. Jedes der Segmente kann seinen Ursprung haben in der verschiedenen Population der Neurone und ausgelöst sein durch eine unterschiedliche Sinneszellart.

2. Bei Mittelohrschwerhörigkeit scheint die Änderung in der Latenz und der Amplitude proportional zu sein dem Grad des Hörverlustes.

3. Bei der Innenohrschwerhörigkeit sollten drei Punkte als grundsätzliche Kriterien für den klinischen Gebrauch beachtet werden) die Gesamtreduktion der Amplitude von N b) die gleichförmige Anstiegsform der Eingangs Ausgang funktion von N_1, mit anderen Worten das Verschwinden der L Kurve us der Eingangs Ausgangs-Beziehung, und) die verlängerte Latenz von N_1

4. Unsere Befunde am AP beim Menschen sind offenbar weitgehend identisch mit jenen, die om Meerschweinchen und von der Katze bekannt sind.

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MYOGENIC EVOKED POTENTIAL RESPONSES TO CLICKS IN MAN

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Human myogenic potentials evoked by clicks have been recorded, both from the external acoustic meatus and from the post auricular region by means of an average response computer. The configuration of the response was triphasic: a negative-positive-negative wave with extremely short latency of the peaks (about 10 to 25 msec). The focus of the response seemed to be localized restricted area of the post auricular region. It was a relatively consistent and low threshold response. The magnitude of the response was amplified to a great extent by the forward flexion of the neck. The post auricular response was interpreted to be cochleo-myogenic in origin.

In short, the post auricular response could be used as an indicator of objective audiometry. Furthermore, in principle, there is a possibility that the response may be applied in an electrophysiological method of differentiating various oto-neurogenic disorders associated with lesions in the brain stem.

INTRODUCTION

Since the human "fast" evoked response to acoustic stimuli was first recorded extracranially by means of an averaging or summing computer method which was originated by Geisler et al (1958), and Geisler (1960), various types of fast evoked response have been recorded differently from the scalp, from the neck, and from all the extremities by many investigators (Bickford et al, 1963 a, b, 1964; Kiang et al, 1963; Mast, 1963, 1965; Davis et al, 1964; Jacobson et al, 1964; Cody et al, 1964; Borsanyi, 1964; Borsanyi & Blanchard, 1964; Davis, 1965; Lowell, 1965; Goldstein, 1965; Goldstein & Rodman, 1967; Ruhm et al, 1967; Celesia et al, 1968).

There is, as a matter of fact, much argument among the authors about the origin and pathway of the fast evoked response. Davis and his associates (1964, 1965 a, b, 1966) have already designated a short latency evoked response occurred during the first 50 msec following an acoustic stimulus as the "fast" evoked response, in order to make a clear contrast to a long latency evoked response with a peak latency of 60 to 300 msec which was called the slow vertex potential evoked

The subject was seated comfortably in a reclining chair in a sound proof room. Usually the head was held natural in an upright position during a test run of 3 to 5 minutes. For the purpose of alterations in the muscular tone or tension of the head and neck muscles, he was instructed either to hold down the head as low as possible, or to hold the head well back during the test run when necessary No extrinsic traction was applied to the head in any direction by means of mecha nical maneuvers. As a result of these head positions, forward and backward flexions of the neck were obtained Additional observations were carried out on a few subjects who lay in a supine position on a bed, resting the head on a pillow

Usually needle electrodes for EEG recording were applied to the subjects. It was inserted hypodermically 5 mm to 10 mm from the surface of the skin at the recording site and then it was fixed firmly on the same place with an adhesive silicon tape for medical use. In case of necessity disc electrodes with EEG jelly were used for an active electrode. It was held in place on the skin with the same adhesive tape.

Active electrodes were placed at various portions of the periauri cula region including the external acoustic meatus, with a reference electrode placed on the ear lobe. A ground electrode was placed on the center of the forehead The distribution of the active electrode will be shown later in the section dealing with the experimental results.

Recording apparatus comprised basically four components a bio medical amplifier (SAN'EI MPA 203 TOKYO), an average response computer (SAN'EI, MEDIAC 401 TOKYO), an oscilloscope (IWASAKI DS 5015, TOKYO), and a photographing system (CANON PHOTO OSCILLOSCOPE UNIT TOKYO).

Electrical responses picked up from the electrodes were led into the amplifie with a flat frequency characteristic from 20 Hz to 500 Hz. The output of the amplifier was fed into the average response computer with an analysis time of 6_5 msec or 125 msec. The computer summed on line in sequence 200 to 500 samples of the amplified electrical response to each of the acoustic stimuli. The summed waveform of the responses to 200 500 clicks was displayed on the oscilloscope and photographed by a 35 mm camera

Stimulating apparatus comprised basically four components a pulse generator system NIHON KOHDEN MSE-40 TOKYO), and audio amplifier SONY 3120 A TOKYO), an attenuator and electroacoustical transducers composed of n electrically shielded earphone and a shielded loud peaker

Acoustic stimuli were clicks originating from a square pulse of 0 1 msec duration prod ced by the pulse generator system. Clicks were gi en either monaurally through the earphone or binaurally through

response In general the fast evoked response may be regarded as a composite response of myogenic evoked potentials and neurogenic evoked potentials (Mast, 1963 1965 Davis et al 1964 1966 Ruhm et al 1967). However on the basis of convincing evidence reported by Bickford et al (1963 a b 1964), and Cody et al (1964), currently the view is widely held that the major component of the fast evoked response is myogenic in origin and the name *sonomotor response*" or "audiomotor response was by them suggested to designate the response.

Apart from the puzzling problem concerning the physiological significance of the sonomotor response, there is still the question whether it is valid and reliable as an indicator of hearing suitable for clinical audiometry

Nowadays at least three types of sonomotor response have been differentiated viz. (1) the inion response (Bickford et al 1964 Cody et al 1964), (2) the short latency vertex and parietal response (Mast, 1963 1965 Goldstein 1965 Goldstein & Rodman 1967), and (3) the post auricular response (Kiang et al 1963 Jacobson et al 1964). As to clinical application Bickford et al (1964) maintained that the inion response can not be used as a valid index of hearing function because the reflex is likely to originate from the vestibular but not the cochlear receptors of the labyrinth In addition the inion response is a high threshold response

In regard to the short latency vertex and parietal response, Mast (1965) observed that it was much more stable and constant at moderate stimulus levels than was the inion response. Recently Goldstein & Rodman (1967) have obtained evidence that it may be of great value in determining threshold sensitivity in man Lowell (1965), however stated that the slow Vertex potential response seemd to serve much better than the fast evoked response

Finally the post auricular response as first reported by Kiang et al (1963), was a variable but low threshold response There is as yet little information as to whether the response can be used to measure human hearing function

Recently we also have observed that the same response, recorded at the external acoustic meatus and the post auricular region is a relatively consistent response, sensitive to weak acoustic stimuli For this reason we will describe characteristics of the post auricular response and its interpretation

METHODS

Observations on the post auricular response were carried out on a number of normal hearing adults and a few patients who suffered from severe sensorineural deafness associated with normal vestibular function

The subject was seated comfortably in a reclining chair in a sound proof room. Usually the head was held natural in an upright position during a test run of 3 to 5 minutes. For the purpose of alterations in the muscular tone or tension of the head and neck muscles, he was instructed either to hold down the head as low as possible, or to hold the head well back during the test run when necessary. No extrinsic traction was applied to the head in any direction by means of mechanical maneuvers. As a result of those head positions, forward and backward flexions of the neck were obtained. Additional observations were carried out on a few subjects who lay in a supine position on a bed resting the head on a pillow.

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Active electrodes were placed at various portions of the *periauricular* region including the external acoustic meatus, with a reference electrode placed on the ear lobe. A ground electrode was placed on the center of the forehead. The distribution of the active *electrode* will be shown later in the section dealing with the experimental results.

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Electrical responses picked up from the electrodes were led into the amplifier with a flat frequency characteristic from 20 Hz to 500 Hz. The output of the amplifier was fed into the average response computer with an analysis time of 62.5 msec or 125 msec. The computer summed on line in sequence 200 to 500 samples of the amplified electrical response to each of the acoustic *stimuli*. The summed waveform of the responses to 200-500 clicks was displayed on the oscilloscope and photographed by a 35 mm camera.

Stimulating apparatus comprised basically four components: a pulse generator system (NIHON KOHDEN MSE-40, TOKYO), and audio amplifier (SONY 3130-A, TOKYO), an attenuator and electroacoustical transducers composed of an electrically shielded earphone and a shielded loud speaker.

Acoustic stimuli were clicks originating from a square pulse of 0.1 msec duration produced by the pulse generator system. Clicks were given either monaurally through the earphone or binaurally through

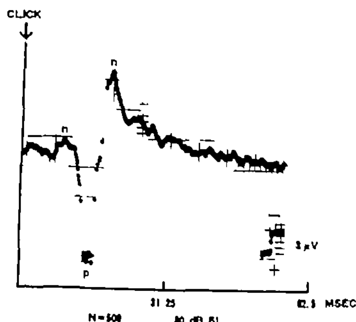


Figure 1 Summed waveform of the myogenic evoked response recorded from the post auricular region (just behind the pinna). Responses to 500 clicks were summed by the computer The subject, a normal hearing young adult, was seated in a reclining chair holding his head in a natural upright position. In this and the rest of the figures, upward deflection indicated negativity of the active electrode (the post auricular region or the external acoustic meatus) with respect to the ear lobe.

the loudspeaker located at a distance of 1 m in front of the subject Unless otherwise stated the interval of acoustic stimulation was 250 msec (4 clicks per second). The intensity of clicks was conveniently represented in terms of sensation levels (SL), i e. decibels above subjective threshold for each subject. The subjective threshold for clicks was measured for all the subjects befor the physiological examination

RESULTS

As a result of click stimulation a short latency evoked response during the first 30 msec after the acoustic stimulus was recorded both from the external acoustic meatus and from the post auricular region in normal hearing subjects The response was easily and consistently recorded when the subject was either seated in a chair holding his head upright or lying on his back on a bed resting his head comfortably on a pillow

Figure 1 illustrates a typical summed waveform of the response consisting of three deflections i e the first negative deflection with a peak latency of 8 to 15 msec the first positive deflection with a peak latency of 13 to 20 msec, and the second negative deflection with a peak latency of 20 to 30 msec respectively with reference to the ear lobe These deflections (peaks) are conveniently designated by the

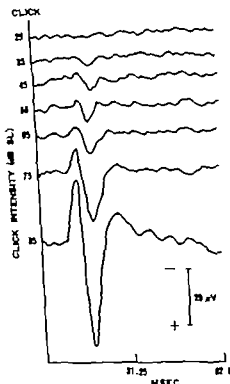


Figure 2. Summed post auricular responses to clicks as function of the stimulus intensity. Each trace is the summed waveform of responses to 500 clicks. The subject, a normal hearing 23-year-old male was seated in chair holding his head in natural upright position. The active electrode was placed just behind the pinna.

symbols of small letters n_1 p_1 and n_2 respectively in order to avoid confusion with the peaks of the slow Vertex potentials represented by the capital letters P_1 N_1 N_2 etc. (*cf* Davis and his associates, 1964 1966). The mean peak latencies at high click intensities above 60 dB SL were about 12 msec for the n_1 about 16 msec for the p_1 and about 25 msec for the n_2 The positive peak, p_1 was most prominent among these peaks. There were slight individual differences in latency but the response obtained from the same place in the same individual gave stable and reproducible latencies of the peaks. As the click intensity increased from a threshold level up to high levels of more than 100 dB SL, the peak latency was reduced to a small extent by about 3 to 5 msec. A prolongation of the latency was distinct near threshold levels.

As shown in Figure –, there was a general trend that the peak to peak amplitude such as the n_1 to-p_1 amplitude or the p_1 to n_2 amplitude was increased with the increase of the click intensity The increase of the amplitude was rapid and remarkable at higher

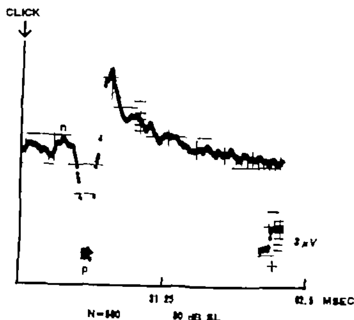


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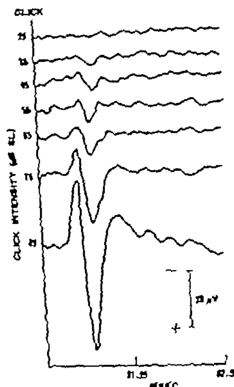


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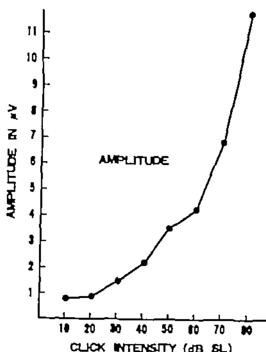


Figure 3. Amplitude (the p_1 to n_1 peak) of the post auricular response as a function of click intensity. Each point is the average of amplitudes for 8 normal subjects.

intensities than 50 to 60 dB SL. Such a rapid growth of the amplitude at high intensities of clicks appeared to be characteristic of the post auricular response.

The magnitude of the post auricular response even to an identical acoustic stimulus varied to a great extent across subjects, across states of the subject and across electrode placement. For this reason it must be borne in mind that a conventional representation of the input output function of the amplitude as demonstrated in Figure 3 is nothing but a rough approximation of the growth of the curve. This input output curve was determined by averaging the data on 8 normal subjects. The slope of the curve is very rapid at high intensities above 60 dB SL.

Figure 4 exemplifies a raw waveform of the post auricular response in a single sweep of the oscilloscope. Such a single response was frequently recorded in a limited area just behind the pinna for an intense click stimulus, from a subject flexing his head and neck in a forward direction. No response to moderate and weak stimuli was seen in a single sweep of the oscilloscope.

The response threshold was defined as the intensity (dB SL) at which the summed response to 500 clicks could be visually detected from background noise of the tracing. For the post auricular response it ranged from 0 dB SL to 20 dB SL in normal hearing subjects.

The magnitude of the response varied from subject to subject. For

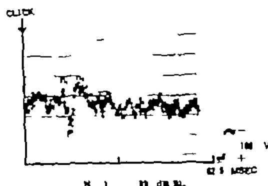


Figure 4. Single response to one click recorded from the post auricular region. The subject, a normal hearing young adult, held down his head as low as possible. The active electrode was placed just behind the pinna. This was photographed from single sweep of the oscilloscope.

example, at an intensity of 90 dB SL the n_1 to p_1 amplitude ranged from 5 microvolts to 100 microvolts across subjects, and at an intensity of 30 dB SL it ranged from 1 microvolt to 5 microvolts.

Figure 5 shows the fast evoked response recorded from the posterior wall of the cartilaginous portion in the external acoustic meatus as a function of click intensity. The configuration of the response is the same as that recorded from the post auricular region.

The whole nerve action potential response (AP) of the cochlear nerve appears simultaneously in the tracing (Figure 5). The AP was prominent at the osseous portion of the external acoustic meatus particularly near the tympanic membrane, whereas the fast evoked response identical with the post auricular response, was strongest at the cartilaginous portion of the external acoustic meatus, particularly at its posterior wall. Usually the amplitude of the fast evoked response was much larger than that of the AP. Moreover it showed a more rapid growth of amplitude as a function of click intensity in comparison with that of the AP as shown in Figures 3 and 5.

Figure 6 is a typical map of the post auricular response over the head in a normal subject. The largest response is recorded both from the limited area just behind the pinna and from the posterior wall of the cartilaginous portion in the meatus. It is distributed widely over the head attenuating its amplitude as a function of the distance between the electrode and the focus of the response. The source of the post auricular response may be localized to the post auricular region as pointed out by Jacobson et al (1964). The response is detectable both from the inion and from the vertex but the amplitude is much reduced. In a few subjects a short latency response, identical with the post auricular response except for a prolonged latency was

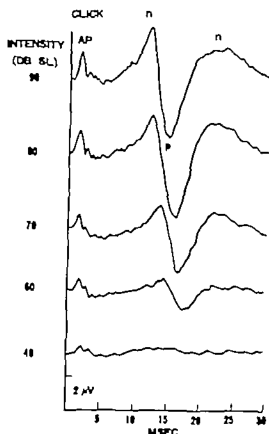


Figure 5 Summed responses to clicks recorded from the e ternal acoustic meatus in a young normal subject. Each trace is the summed waveform of responses to 500 clicks, The active electrode was placed at the posterior wall of the cartilaginous portion of the external acoustic meatus. Both the AP and the post auricular response (n p₁ n₂) are seen each trace

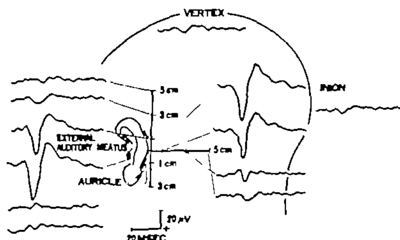


Figure 6 Summed post uricul responses to cli ks recorded from variou lectrod position on tl e scalp The subject 31 y ar old mal with normal hearing, wa seated in a chair holding his head i nat ral upright posit on The li k int nsity wa 00 dB SL. Responses to 500 click w re summed by th computer The beginning on the l ft sid) of each trace indi ates th rri al of li k nd the tart of the trace

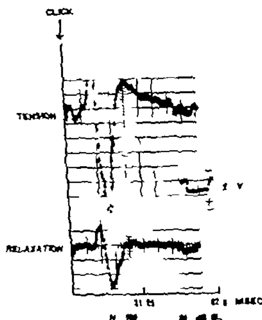


Figure 7 Positi effect of muscular tension on the post auricular response to licks. The subject, a 17 year-old male with normal hearing was seated i chair either flexing the head and neck forward (upper tracing) or holding the head in natural upright position (lower tracing). Each tracing i the summed waveform of responses to 500 licks. Marked amplificat on in magnitude of the response is seen in the upper tracing.

recorded from the arms and the legs.

These distributions of the post auricular response on the head are practically identical with those reported by Kiang et al (1963), and Jacobson et al (1964).

The post auricular response was a bilateral response to monaural a oustic stimuli. When the *antlateral* ear alone was stimulated by clicks th ough an earphone, the response could be recorded simultane ously on both sides in the *post auricular* regions.

Figure 7 illustrates a positive *effect of* muscular tension of the head and the neck on the magnitude of the response. Forward flexion of the neck was very effective for increasing the response. The ampli tude was highly enhanced by holding down the head as low as possible. In general holding the head back well decreased the amplitude of the post auricular response, in comparison with holding the head naturally in an upright position The degree of amplification of the mplitude in the forward flexion of the neck ranged from about 3 times to 10 times as large as that obtained in an upright position. When the subject lay in a supine *position* on a bed the use of a pillow resulted in an ffect similar to *that* of forward flexion of the neck These findings are in close agreement with those observed on the inion

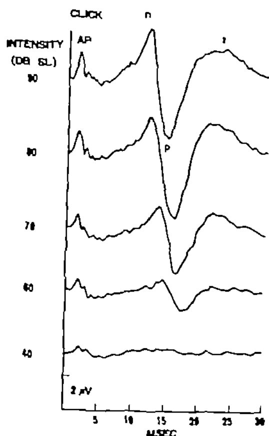


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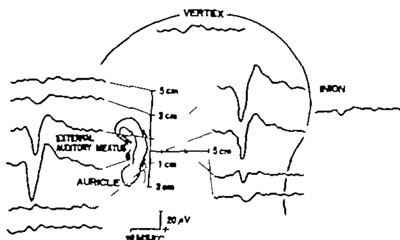


Figure 6. Summed post auricular responses to li ks recorded from ariou electrod position on the scalp The subject 34 year old mal with normal hear g wa seated in a chair holding h s head in natural pright posit on The lick t nsity wa 60 dB SL. Responses to 500 clicks were summed by the comput The beginning (on the left sid) of ea h trace indicates th rri al of li k and th t rt of the trace

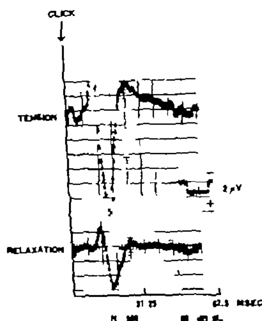


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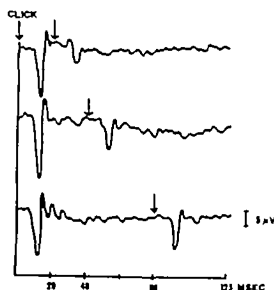


Figure 8. Summed post auricular responses to paired clicks recorded from a normal hearing subject holding his head in a natural upright position. Responses to 200 clicks with an intensity of 75 dB SL were summed by the computer. The ordinate marks the arrival of the first clicks and the start of the trace. The later arrows indicate the onset of the second click at various intervals after the first clicks.

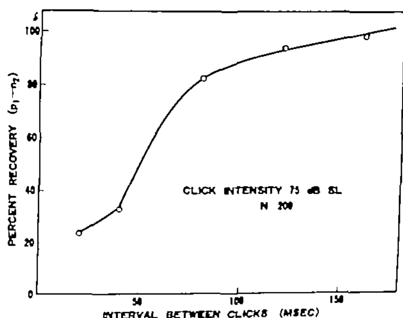


Figure 9. Recovery curve of amplitud (p₁ to n₄) of the post auricular response. Each point is the average of measurements of the percent recovery for 3 normal subjects. Responses to 200 clicks were summed by the comput r. The active electrode w placed behind the pinna. The subject was seated in a chair holding his head in a natural upright position. Th percent recovery is the ratio, expressed as percentage of th second response to that of the first response.

response (Bickford et al 1964), and on the short latency vertex and parietal response (Mast, 1963, 1965).

Figure 8 is an example of the post auricular responses to paired clicks of the same intensity in which the first click is separated from the second by a short interval. The paired clicks are presented at a long interval of 500 msec, independently of the short interval. The amplitude of the second response is gradually reduced as the short interval decreases.

Figure 9 is the mean recovery function determined on 3 normal subjects of the p_1 to n_2 peak amplitude of the second response in relation to that of the first response as a function of the short interval. The percentage of the amplitude of the second response to that of the first one is plotted on the ordinate. The recovery curve rises rapidly from a recovery level of about 20 per cent at the interval of 20 msec to a recovery level of 90 per cent at the interval of 100 msec, and then it increases very slowly towards a recovery level of 100 per cent. The short interval necessary for full recovery may approximate 200 msec. The time course of the recovery process of the post auricular response appeared to be much faster than that of the slow Vertex potential evoked response, but slower than that of the AP

Finally we have recorded no response to intense clicks at intensities above 100 dB SPL (peak equivalent) from the post auricular region in patients who suffer from severe sensorineural hearing loss but with normal vestibular function Strong flexion of the neck in a forward direction was not effective in evoking the response from these patients. This may be contradictory to the observations on the inion response (Bickford et al 1964 Cody et al 1964), but is compatible with those reported by Ruhm et al (1967).

DISCUSSION

Characteristics of the fast evoked responses recorded from the post auricula region and the external acoustic meatus

On the basis of the above observation it is clear that our responses are essentially identical with the post auricular response of Kiang et al (1963). The distribution of the response on the scalp is also in close agreement with that reported by Jacobson et al (1964). High sensitivity to acoustic timuli may be a feature worthy of special mention in the post auricular response in contrast to the inion response which has a high threshold Additional features are the ease of recording the response and its stability

Cli ical significance of the Fast Evoked responses

The hypothesi of a widespread sonomotor response system in man,

as first put forward by Bickford et al (1963 a b), has been generally accepted by many investigators (cf Cody et al 1964 Davis et al 1964 Davis 1965 Celesia et al 1968 Ruhm et al 1967 Borsanyi 1964 *Borsanyi & Blanchard 1964*). Recently an interesting explannation regarding the mechanisms and pathways of the fast evoked responses was offered by Ruhm et al (1967), *namely that there may be a dual* system operating in the same time domain comprising a cochleo neurogenic system which has a low threshold and a vestibulo myogenic system which has a high threshold By extension of the dual organi sation theory of Ruhm et al (1967), it would be reasonable to speculate that the fast evoked response may be a mixed response consisting of (1) a cochleo myogenic response (2) a cochleo neurogenic response, and (3) a vestibulo myogenic response. But actually such a triple organi sation in man has not yet been demonstrated

In the light of the experimental evidence collected by the authors, as mentioned earlier in the introduction the following inferences may be of interest (1) The *major component of the post auricular response* may be interpreted to be cochleo myogenic in origin (2) The inion response of Bickford et al (1964), and Cody et al (1964), may be vestibulo myogenic in origin (3) The short latency vertex and parietal response may be a composite response consisting of the cochleo neurogenic component (Mast, 1963 1965 Davis 1966 Goldstein 1965 Ruhm et al 1967), the cochleo myogenic component (Mast 1963 1964 Davis, 1966 Goldstein & Rodman 1967), and the vestibulo myogenic response (Ruhm et al 1967 Cerecia et al 1968).

As regards the cochleo neurogenic component of the fast evoked response Davis et al (1966), in support of the view of Mast (1963, 1965), have suggested that a small early neurogenic auditory response of a 30 msec peak latency might be detected in appropriate area in additon to the sonomotor response but the overwhelming myogenic response made it very difficult to detect

Audiometric use of the fast evoked responses

Among a group of fast evoked responses the inion response would not serve as an index of *hearing estimation because of the vestibular* mediation as described by Bickford et al (1964), and Cody et al (1964).

On the other hand as both the post auricular and the short latency vertex and parietal responses seem to be evoked by cochlear receptors they would be valid for objective audiometry These responses have been proved not only to be relatively stable and consistent but also to have a low threshold according to Kiang et al (1963), Mast (1965), Borsanyi *(1964), Ruhm et al (1967 Goldstein* (1965), and Goldstein & Rodman (1967). Our findings on the post auricular response *support the* view of Goldstein & Rodman (1967) that audiometric use

of the fast evoked response, for "objective" measurement of hearing threshold in man may be promising.

As cited earlier Bickford et al (1964) have also pointed out the theoretical importance of the human sonomotor response in differentiat ing vestibular disease.

Apart from threshold measurements, another point of interest is that the myogenic evoked potentials, irrespective of the receptors (vestibular or cochlear), may be of practical value in differential diagnosis of oto neurological diseases in the brain stem. Davis (1965) has already emphasized that the myogenic evoked potentials may serve to differentiate failure of response due to lesions of the brain stem from impairment of the cochlea or of the brain cortex.

As a matter of fact, in view of possible diagnosis of central perceptive deafness it is reasonable to accept this suggestion. Theo retically the myogenic evoked potentials may be applicable to differ ential diagnosis of auditory and vestibular diseases in the brain stem region but much remains to be determined as to the anatomical pathway and physiological function of th resoponse

ACKNOWLEDGEMENTS

W wish to express our gratitude to the Director of the Department of Oto-laryngology Professor Tokuro Suzuki Shinsh University Matsumoto for his encouragement and generous support throughout the entire investigation.

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ZUSAMMENFASSUNG

Nach Click Reizung wurden die myogenen evoked potentials beim Menschen sowohl am äusseren Gehörgang als auch etroaurikulär mit Hilf eines Mittelwertre chners registriert. Die Antworten st llten sich ls dreiphasische W lle da und war als neg tiv positi negati Welle mit einer extrem Latenz der Spitzen (10-15 23 msec). Der Herd dieser A tworten ist offenbar in einem umschriebenen retroaurikulären Bezirk gelegen. Die Schw lle der Antworten war relativ konstant und iedrig. Durch Vorwärtsneigen des Kopfes liess sich die Grösse der Antworten erheblich steigern. Die postaurikulären Antworten werden i terpretiert als cochleo-myogenen Ursprungs. Sie lassen sich gut fur die objektiv Audiometrie verwenden. Ausserdem besteht grundsätzlich die Möglichkeit dass die Antworten für elektro-phy iologische Versuche erwendet werden konnen zur Differenzierung erschiedener otoneurologischer Störungen im Zusammenhang mit Schädigungen des Hirnstamms.

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ACTA OTO LARYNGOLOGICA

SUPPLEMENTUM 251

From the Department of Physiology Section of Neurophysiology Baylor College of Medicine, and The Methodist Hospital, Houston, Texas, U.S.A

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CONTENTS

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CONTENTS

INTRODUCTION

It is generally agreed that "vestibular neuronitis" is an abnormality of the vestibular system without an accompanying auditory deficit. It is also generally agreed that vestibular neuronitis is frequently associated with an infectious process and that it tends to occur in relatively young adults. Beyond this, however there is little agreement concerning the precise delineation of what constitutes "vestibular neuronitis."

Proponents of differing views tend to form two distinct groups. The first group accepts a rather broad definition of vestibular neuronitis, including ither multiple or single attacks of vertigo or dizziness, and any type of abnormality disclosed by vestibular examination. The second group accepts a more limited concept of what comprises vestibular neuronitis, maintaining that there is only a single usually very severe, episode of vertigo, that the vestibular examination shows a unilateral weakness of the caloric responses, and that, if done early in the course of the illness, it also shows a spontaneous nystagmus directed away from the unilateral weakness. These investigators uniformly regard the entity as self-limiting, whereas those using the broader definition disagree about this point

The condition was originally described by Dix and Hallpike in 1952 Their criteria provide an example of the broader definition, as they characterized the attacks f vertigo or dizziness as either multiple or single and reported that of their 100 cases, 47 had bilateral canal paresis and 53 had unilateral canal paresis. They also reported that the condition "generally ceases within a few years. The following investigators have also used the broad definition Harrison (1962) studied 67 patients conforming to the original description by Dix and Hallpike and found that in 29 the attacks were repeated over periods up to 7 years. No spontaneous nystagmus was encountered in this series. Lumio and Aho (1965) studied 40 patients with "vestibular neuronitis, and found that f 27 patients followed for at least 6 months, all showed complete recovery or only mild, recurrent unsteadiness. Boffi (1965) reported on 85 cases with a diagnosis of vestibular neuronitis according to the definition of Dix and Hallpike" He postulated a relationship between vestibular neuronitis and paroxysmal positional nystagmus, which Lindsay (1967) also suggested. Lindsay preferred to reserve the term, "vestibular neuronitis, for patients with a "vestibular disturbance of inflammatory origin in which definit localizing signs are lacking

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the acute stage shows "a gross vestibular nystagmus The quick component is directed towards the sound side At the end of three weeks the nystagmus has disappeared and equilibrium is more or less restored" Dolowitz (1965) characterized vestibular neuronitis as a sudden acute vestibular failure affecting all or part of the [peripheral vestibular apparatus] This disease is characterized by an apparently normal person suddenly being seized with violent vertigo, nausea and vomiting any time that the head is moved The only pathological signs are the decreased labyrinthine responses. [The disease] is self limiting Lachman and Stahle (1967) studied 45 *cases of vestibular neuronitis" in the acute stage In all cases the vertigo* had a precipitous onset The caloric test showed a [unilateral] canal paresis in all cases and a vigorous spontaneous nystagmus away from the canal paresis." The disease was characterized as having a 'protracted course from weeks to months.

Hart (1965) recognized within the original broadly defined syndrome an entity essentially identical to that of the more restricted definition but preferred to call it "vestibular paralysis of sudden onset and probable viral etiology He reserved the term 'vestibular neuronitis, for all other cases of vestibular derangement without associated auditory deficit Of particular importance is Hart s suggestion that whether single or multiple episodes of vertigo are present represents an important criterion for subdividing the syndrome of 'vestibular neuronitis as originally described by Dix and Hallpike

It is noteworthy that investigators utilizing the electronystagmographic (ENG) examination to provide diagnostic criteria tend to adopt the more restricted definition The ENG examination thus may provide worthwhile information not given by other diagnostic procedures

The present study was undertaken in an attempt to clarify the confusion surrounding the definition of vestibular neuronitis by establishing precise and limiting diagnostic criteria for the entity A group of patients fulfilling these criteria were then analyzed to determine the significance of other clinical findings in the group

SECTION I DEFINITION OF VESTIBULAR NEURONITIS

MATERIALS AND METHODS

We approached the problem of defining the vestibular neuronitis in the following way First, we tried to determine whether various characteristics supposed to typify the entity were significantly more prevalent among patients with a vestibular deficit but without an auditory deficit than among control patients (i.e. those with both a vestibular and an auditory deficit, and those with normal auditory and vestibular function) Second, we studied the group of patients with a vestibular deficit and normal hearing to determine whether it was completely homogeneous or whether it could be divided into subgroups of patients with and without vestibular neuronitis. We subdivided the group into patients with single and patients with multiple episodes of vertigo to see whether the various characteristics supposedly typical of vestibular neuronitis were significantly more prevalent in one of the subgroups than in the other Single- and multiple-episode subgroups of the control groups were also compared to rule out the possibility that differences between the study subgroups were due solely to the presence of single episodes of dizziness in one subgroup and multiple episodes in the other

The patients studied were obtained from 1346 consecutive patients referred to the electronystagmographic laboratory at The Methodist Hospital in Houston, Texas.

To be included in the study it was required that a patient complain of dizziness, defined as something equivalent to giddiness or light headedness as well as a spinning sensation, and also that he meet the criteria of one of the three study groups, defined below A total of 604 patients fulfilled these criteria.

Control group 1 Normal

Included in this group were 418 patients with caloric unilateral weakness and directional-preponderance measurements of less than 20% without spontaneous or positional nystagmus, and without optokinetic asymmetry or gaze nystagmus.

Control group 2 Caloric unilateral weakness with correlated auditory deficit (udit ry nd vestibul r" or "A & V")

The 110 patients in this group had unilateral-weakness measurements of 20 or more and had a hearing loss, by history on the same side or when

audiogram was available (94 patients) had a difference in hearing level of at least 20 db (averaged over the 500–2000 Hz range).

Study group. Caloric unilateral weakness without significant hearing loss (vestibular-only or V-only).

The 76 patients in this group had unilateral weakness measurements of 20% or more and had normal hearing by history or, when an audiogram was available (36 patients), had an average hearing level over the 500–2000 Hz range of 20 db or less in both ears.

All of the 604 patients were given an ENG examination which consisted of a test for gaze nystagmus with eye deviation quantitated at 20° from the midline, an optokinetic test, a position test according to Aschan et al.'s (1956) modification of Nylén's technique, and a Fitzgerald-Hallpike (1942) caloric test.[1] The caloric responses were quantitated by measuring maximum eye speed. Directional preponderance (DP) and unilateral weakness (UW) were expressed as a percentage of the total of all four caloric responses. "Limit of normal" (determined by doubling the standard deviation obtained from a series of normal subjects) was 20% for both UW and DP. Additional details of the test procedure are published elsewhere (Coats, 1965, 1966).

A complete otoneurologic history was obtained from all of the patients. In addition, a vigorous effort was made to obtain records from referring physicians, from hospitals (if the patient was an in-patient at the time of the examination) and of test results pertinent to the otoneurologic examination, particularly of audiometric examinations.

RESULTS

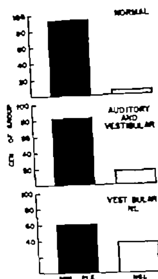
Comparison between the V-only group and the two control groups

Multiple and single episodes of vertigo. For this study, a single episode of vertigo was defined as one or a series of attacks occurring within a 10-day period. Episodes not fitting this definition were regarded as multiple. In Fig. 1 are plotted the incidences of single and multiple episodes in the three groups.

It is apparent that the incidence of single episodes is much higher in the V-only group than in either of the control groups. This difference is statistically significant (see Appendix I). However, in the V-only group, multiple episodes outnumbered single episodes. Similar observations have undoubtedly led others to conclude that "vestibular neuronitis" may be manifested by either multiple or single episodes of dizziness.

Age distribution. Distributions of patients' ages in the three groups are shown in Fig. 2. It is apparent that patients with V-only deficit tended to be

[1] We have recently begun to use temperatures of 31°C and 43°C (irrigation duration 40 seconds) rather than 30°C and 44°C. We find that this method of reducing stimulus intensity is better than shortening the duration of the irrigation (Aschan et al. 1956) because shortening the duration increases the variability of the response.



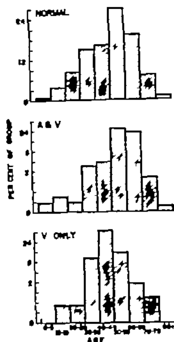


Fig. 1

Fig. 2

Fig. 1 Percentages f patient i the three groups complaini g of m ltipl nd singl episodes of dizziness.

Fig. 2 Ag distributi ns in the three patient groups.

younger than patients in the control groups. This difference is highly significant (see Appendix, II) There was no significant age difference between the two control groups.

Incidence of anteced nt infection (Table 1) The incidence of infection during the two months prior to the ENG examination was as follows (Fig 3) (1) in the V-only group, 29 of 6 patients (38.2%) (2) in the A & V

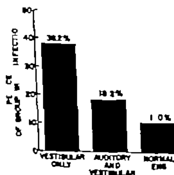


Fig. 3 Percent ges of patient in the three groups with history of infection within two month prior t the ENG examination.

Table 1 *Antecedent infection in patient groups*

	Normal				A & V				V-only			
	Multiple attacks (391 patients)		Single attacks (27 patients)		Multiple attacks (91 patients)		Single attacks (19 patients)		Multiple attacks (47 patients)		Single attacks (29 patients)	
Type of infection	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Upper respiratory	6	1.5	1	3.7	0	0	2	10.5	1	2.1	3	10.3
Sinusitis	12	3.1	0	0	4	4.4	0	0	9	19.1	1	3.4
Middle ear	5	1.3	1	3.7	5	5.5	2	10.5	3	6.4		6.9
Flu	5	1.3	0	0	1	1.1	0	0	1	2.1	2	6.9
Specific viral	3	0.8	0	0	2	2.2	2	10.5	1	2.1	1	3.4
Other	8	2.0	1	3	1	1.1	1	5.3	1	2.1	4	13.8
Total	39	10.0	3	11.1	13	14.3	7	36.8	16	34.0	13	44.8

Definitions

Upper respiratory = "cold" and/or "sore throat"

Sinusitis = sinusitis or sinus congestion diagnosed by referring physician.

Middle ear = symptoms and/or signs of chronic or acute middle-ear infection which had been active within two months of examination

Flu = febrile illness, usually associated with upper respiratory infection which could not be classified as a specific viral infection

Specific viral = measles, mumps, chicken pox, herpes zoster and "meningoencephalitis"

Other = a wide variety of types which could not be classified according to the above criteria most infection by bacteria or other non-viral organism were included in this category

group 20 of 110 patients (18.2%) and (3) in the normal group 42 of 418 patients (10.1%) The incidence in the V-only group was significantly higher than that of the control groups (see Appendix III) The incidence in the A & V group was significantly higher than in the normal group This difference was largely attributable to higher percentages of patients with middle-ear and specific viral infections in the A & V group

Other etiological factors Other etiological factors were studied in an attempt to demonstrate a significantly higher concentration in the V-only group in comparison with the control groups However none of the possibilities studied (diabetes, head trauma, vascular insufficiency streptomycin intoxication barotrauma, and bleeding episodes) occurred significantly more often in the V-only group This negative result does not exclude the possibility that a significant positive result might be produced by study of a larger population

Incidence of spontaneous nystagmus Of the 76 V-only patients, 61 (46 patients) had spontaneous nystagmus. Only 44% (48 patients) of the 110 A & V patients had spontaneous nystagmus. This difference is statistically significant (see Appendix IV) As will be shown the high incidence of spontaneous nystagmus among the V-only patients is attributable entirely to

the high incidence of spontaneous nystagmus among patients with single episodes of dizziness.

Conclusion A group of patients with a vestibular deficit but without a corresponding auditory deficit differed significantly in several respects, from a group of normal patients and from a group of patients with both vestibular and auditory deficits. The V-only patients tended to be younger had a higher incidence of antecendent infections and spontaneous nystagmus, and more of them complained of only a singl episode of dizziness. These findings suggest that the V-only group contained a high concentration of a particular entity (vestibular neuronitis) which has these characteristics. However these findings by no means prove that the V-only group contained only this entity If the V-only group could be subdivided according to some predetermined criterion, and the subgroups shown to differ significantly in one or more respects, then it would seem doubtful that patients with a vestibular deficit, but without an auditory deficit, constitute a homogeneous group As shown in the following section, V-only patients with only a single episode of dizziness differed significantly in several respects from V-only patients with multiple episodes of dizziness.

Comparison of multiple- and single-attack subgroups

Age distribution. In Fig 4 are shown the age distributions in the six subgroups formed by subdividing the three major groups according to whether their attacks of dizziness were multiple or single The V-only-single-attack subgroup was the youngest, with a modal age of 30–39 The V-only multiple attack subgroup was significantly older than the V-only single-attack subgroup, and did not differ significantly in age from the control subgroups (see Appendix, II) In contrast to the V-only group, there were no significant age differences between subdivisions of the control groups.

Amount of unilateral weakness In Fig 5 are shown frequency distribution of amount of unilateral weakness in subgroups of the two groups with unilateral weakness. The UW measurements in the V-only multiple-attack subgroup show a strikingly high percentage at the low end of the scale when compared with the UW measurements in the other three subgroups. This difference is highly significant (see Appendix, V) There are no significant differences among the other three subgroups. Thus patients in the V-only multiple-attack subgroup tend to have significantly smalle UW measure ment than patients in the other subgroups.

Incid nce int nsity and direction of spontaneous nystagmus The incidence of spontaneous nystagmus (nystagmus present with the patient supine and eyes closed) in ubgroups of the two UW groups is shown in Fig. 6 The incidence i highest in the V-only-single-attack subgroup (80%) In Fig 7 the spontaneous nystagmus has been categorized according to intensity and direction relativ to th weak side The V-only-singl -attack subgroup differs in that in all instances where spontaneous nystagmus was present it was directed away from the side of the unilateral weakness, and in the majority

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Type of infection	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Upper respiratory	6	1.5	1	3.7	0	0		10.5	1	2.1	3	10.3
Sinusitis	12	3.1	0	0	4	4.4	0	0	9	19.1	1	3.4
Middle ear	5	1.3	1	3.7	5	5.5	2	10.5	3	6.4	2	6.9
Flu	5	1.3	0	0	1	1.1	0	0	1	2.1	2	6.9
Specific viral	3	0.8	0	0	2	2.2	2	10.5	1	[illegible]	1	3.4
Other	8	2.0	1	3	1	1.1	1	5.3	1	2.1	4	13.8
Total	39	10.0	3	11.1	13	14.3	7	36.8	16	34.0	13	44.8

Definitions

Upper respiratory – "cold and/or sore throat"
Sinusitis – sinusitis or sinus congestion diagnosed by referring physician.
Middle ear – symptoms and/or signs of chronic or acute middle-ear infection which had been active within two months of examination.
Flu – febrile illness, usually associated with upper respiratory infection which could not be classified as a specific viral infection
Specific viral – measles, mumps, chicken pox, herpes zoster and meningoencephalitis
Other – a wide variety of types which could not be classified according to the above criteria most infections by bacteria or other non viral organisms were included in this category

group 20 of 110 patients (18.2%) and (3) in the normal group, 42 of 418 patients (10.1%) The incidence in the V-only group was significantly higher than that of the control groups (see Appendix, III) The incidence in the A & V group was significantly higher than in the normal group This difference was largely attributable to higher percentages of patients with middle-ear and specific viral infections in the A & V group

Other etiological factors Other etiological factors were studied in an attempt to demonstrate a significantly higher concentration in the V-only group in comparison with the control groups However none of the possibilities studied (diabetes, head trauma vascular insufficiency streptomycin intoxication barotrauma, and bleeding episodes) occurred significantly more often in the V-only group This negative result does not exclude the possibility that a significant positive result might be produced by study of a larger population

Incidence of spontaneous nystagmus Of the 76 V-only patients, 61 (46 patients) had spontaneous nystagmus. Only 44 (48 patients) of the 110 A & V patients had spontaneous nystagmus This difference is statistically significant (see Appendix IV) As will be shown the high incidence of spontaneous nystagmus among the V-only patients is attributable entirely to

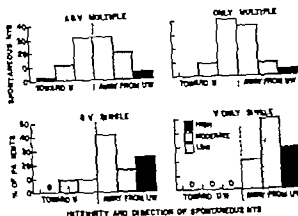


Fig. 7 Percentage distributions f intensity of spontaneous nystagmus nd direction rela t t side f UW. Spontaneous-nystagmus intensity measurement were categorized a low 0.1–6.9 sec; moderat 6.0–9.9°/sec; high 10.0°/sec+

subgroups are significant. This is largely attributable to the relatively high incidence (19 1%) of sinusitis in the V-only multiple-attack subgroup (Fig 8) It was required that sinusitis" or "sinus congestion have been diagnosed by the referring physician before the patient was considered to have this disorder

In contrast to the V-only multiple-attack subgroup all types of infection occurred with approximately equal frequency in the V-only single-attack subgroup The highest incidence was in th "other" category The four patients in this category had the following types of infection positive serol ogy with probable asymptomatic tertiary syphilis, jaundice and fever of un known origin, colitis with diarrhea and fever and bronchitis with fever

Follow-up study Thirty-six V-only patients with UW measurements of 30% or more and with antecedent infection, were contacted 1 to 4 years after the ENG examination. Of these, 20 had only a single episode of dizzi ness. These patients meet the definition of vestibular neuronitis proposed below The remaining 16 patients had multiple episodes of dizziness. Accord ing t many investigators, these patients also have vestibular neuronitis (they have a estibular deficit, normal auditory function, and an antecedent infection) However as proposed below they should be excluded because they had multiple attacks of dizziness.

A short questionnaire was mailed to each patient. The patient was asked whether there had been recurrent dizziness. If so, he was asked to grade the recurrence as "more severe," about as severe, "less severe " or much less severe" than the episode occurring at the time of the examination Also, he was asked whether medical treatment had been sought for recurrent dizzi ness. In addition, the questionnaire provided space for comments."

Of the 36 patients, 26 returned the questionnaire Eight additional patients were interviewed by telephone Two patients were lost to follow-up one

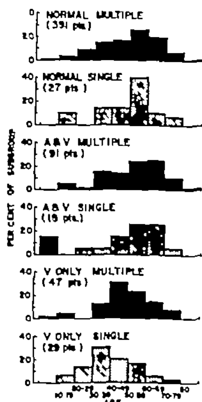


Fig 4

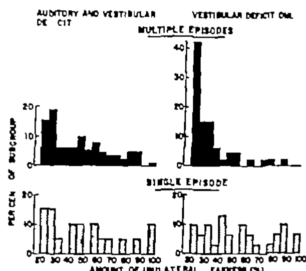


Fig 5

Fig 4 Age distributi n in the six subgroups.

Fig 5 Distribution of cal ric unilat ral weakness measurements in the subgroup f the two groups with unilat ral weakne s.

of instances, was of moderate or high intensity These differences are statisti cally significant (see Appendix IV)

Incidence and type of infection When infection was subdivided according to type, a significant difference between the V only multiple-attack and V only single attack subgroups was found In Table 1 the incidence of differ ent types of infection in the six subgroups is shown Although the overall incidences of infection in the V-only multiple attack and V-only single-attack subgroups (34 0% and 44 8% respectively) do not differ significantly (see Appendix III) differences between the types of infection in these two

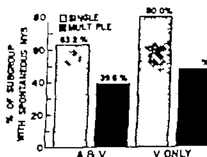


Fig 6 P rcent ges f pati t with spo t eo st gm i th pine positi

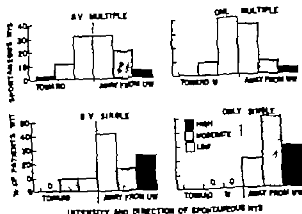


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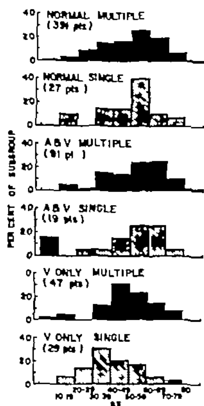


Fig 4

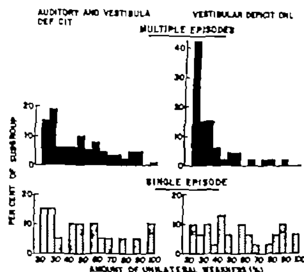


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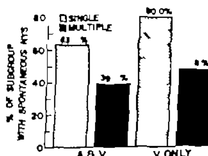


Fig 6 Percent ges of pati nt with pont eou nyst gm in the supine po it n.

"much less severe" dizziness in this group Thus, one patient related a single "much less severe, recurrent episode occurring after she had attended a wedding with a large crowd following lack of sleep the night before" Another patient related a single episode, and stated, "I am sure it was from overwork and no time for eating" A third patient stated that he "gets dizzy" if he goes too fast or stands too long"

In contrast to the single-attack subgroup, none of the patients with multiple attacks offered comments which specifically related recurrent episodes of dizziness to fatigue, emotional stress, or drug ingestion. The only specific cause of recurrent dizziness volunteered by patients in this group was given by two patients who related their recurrent attacks to exacerbations of sinusitis.

DISCUSSION

Differences between the V-only group and the control groups

The results of this study indicate that patients with caloric unilateral weakness without associated hearing deficit (V-only patients) differ significantly from control groups in that (1) they tend to be younger (2) they tend to present with only a single episode of dizziness, (3) they have a relatively high incidence of spontaneous nystagmus, and (4) they have associated infection with much greater frequency

These results support the definition of "vestibular neuronitis" as an entity which is characterized by a vestibular deficit without auditory deficit, usually occurring in a relatively young adult who frequently gives a history of antecedent infection. That the definition should include the stipulation that there be only a single attack of dizziness is indicated by the additional results discussed below

Differences between the V-only multiple-attack and V-only single-attack subgroups

The V-only group with multiple attacks of dizziness differed significantly in several respects from the V-only group with a single attack. The severity of caloric unilateral weakness in the V-only-multiple-attack group tended to be much less than in the single-attack group Also, patients with multiple attacks tended to be older than patients with single attacks (though still younger than the control groups) This is in contrast to the control groups, where patients with multiple and single attacks showed no significant age difference. Also, a follow up study showed a much higher incidence of relatively severe recurrent episodes in the multiple-attack group as compared to the single-attack group. Finally patients with multiple attacks showed a striking tendency to have sinusitis. No such tendency was found in any of the other patient groups. The high incidence of sinusitis among V-only patient with multiple attacks suggests that at least one separate disease entity occurs within this subgroup

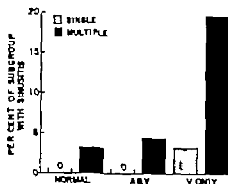


Fig 8

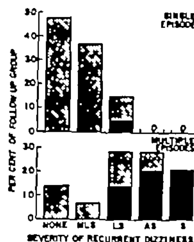


Fig. 9

Fig 8 Percentag s of patients in the six subgroups with sinusitis within two months prior to the ENG examinati n (diagnosed by referring physician)

Fig 9 Recurrent episodes of dizziness in patients *on whom follow-up information was* obtained. Solid bars represent patients seeking medical care for recurrent attacks. Cross-hatched bars represent patient with recurrent atta ks but not seeking medial care The upper plot w obtained from the follow up group meeting the definition of v stibular neuronitis proposed in this rep rt (caloric unil teral weakness without uditory deficit with ingle recent episode of dizziness, and with antecede t infection) The lower plot wa obtained from a group of patients with the same characteristics except that they *presented with a hi tory of multiple episodes of dizziness. None = no recurrent dizziness* MLS = recurrent episode(s) much less severe than initial episode LS = less severe recurrent episod ( ) AS = s severe recurrent episod (s); MS = m re severe recurrent episod (s)

with multiple attacks had died of a myocardial infarction two months after the ENG examination

The results of the follow up study are presented in Fig 9 It is apparent that patients with only a single attack of dizziness at the time of the ENC examination were relatively free of subsequent attacks. In contrast most patients who had had multiple attacks at the time of the ENG examination continued to have relatively severe attacks after the examination

The "comments" which were volunteered by many of the patients provide some interesting insights into probable causes of the recurrent episodes of dizziness and also into differences between the multiple- and single-attack subgroups It is easy to visualize occasional episodes of mild dizziness occurring in a patient with a stable peripheral vestibular deficit caused not by exacerbation of the peripheral lesion but by a temporary unbalancing of the central compensation for the peripheral lesion Fatigue emotional stress, or drug ingestion (e g., alcohol sedatives) would be expected to produce such a temporary "decompensation" Several of the comments volunteered by patients in the single-attack follow up group support the view that this mechanism accounted for many of the recurrent episodes of

patients meeting our proposed definition of vestibular neuronitis. The results of the present study thus suggest that an isolated vestibular deficit associated with sinusitis represents an entity which is distinct from "vestibular neuronitis." The comments volunteered by two of the follow up patients that recurrent episodes of dizziness were associated with exacerbation of their sinusitis are further evidence for this view

Etiologic factors in vestibular neuronitis

It is frequently suggested that vestibular neuronitis may be caused by viral infection. In the present survey a significant relationship between infection and vestibular neuronitis was found, but there was no association with a specific type of infection. Therefore in vestibular neuronitis, infection is probably a secondary rather than a primary etiologic factor

SUMMARY OF SECTION I

A group of 76 patients with peripheral vestibular deficits and normal hearing differed significantly from 528 "control" patients in the following areas (1) younger median age (30–40 vs. 50–60) (2) higher incidence of antecedent infection, (3) higher incidence of spontaneous nystagmus, and (4) greater percentage of patients with only a single attack of dizziness. Among the 76 patients, those with single attacks of dizziness differed significantly from those with multiple attacks in a number of ways therefore, it is suggested that the definition of vestibular neuronitis include the stipulation that there be only a single attack of dizziness. A follow up study showed that recurrent dizziness was rare in patients presenting with only a single episode but was common in patients presenting with multiple episodes. Among patients with multiple episodes, a possibly new entity "isolated vestibular deficit associated with sinusitis," was found. On follow up, two of these patients voluntarily commented that recurrent episodes of dizziness were associated with exacerbations of their sinusitis.

Another possible explanation for the significant difference between the V-only multiple-attack and V-only single-attack subgroups must be considered. It can be argued that the marked tendency for the UW measurements in the V-only multiple-attack subgroup to cluster near the lower limit of the "pathological" range occurs because many of these measurements are in fact spuriously abnormal results. It will be recalled that the 20% limit of normal is determined by doubling the standard deviation obtained from a population of normal subjects. Thus, by definition, about 4.5% of normal individuals will *fall outside this "limit of normal".* Most of the patients with normal ENG's complained of multiple attacks of dizziness. Also, the V-only group by definition constitutes patients with supposedly peripheral vestibular deficits unconfirmed by auditory deficits. Therefore it would be expected that the spuriously *"abnormal" caloric test results would tend to* concentrate in the V-only multiple-attack subgroup.

This consideration constitutes another argument for excluding V-only patients with multiple attacks of dizziness from the same diagnostic classification as V-only single-attack patients. (It is also a strong argument for repeating the caloric test in such patients.)

It is apparent from these results that the V-only single-attack subgroup is relatively homogeneous, being largely made up of patients with what we propose be called "vestibular neuronitis". The V-only multiple attack subgroup is a conglomerate of at least two entities: (1) "spuriously" abnormal unilateral weakness measurements, and (2) a possibly new entity, vestibular deficit associated with sinusitis. The results of this study thus indicate that the definition of "vestibular neuronitis" should include the stipulation that the patient have had only a single attack of dizziness. This stipulation may or may not exclude a few "atypical" examples, but in addition to fitting the data presented here it gives the diagnosis prognostic value.

Vestibular deficit associated with sinusitis

A high incidence of sinusitis in patients with vestibular deficit and normal hearing has been reported by several investigators. In the series of Dix and Hallpike (1952) antral infection was the most frequent type of *infection.* Hinchcliffe (1964) stated that 30 to 50% of patients with vestibular neuronitis have roentgenographic evidence of sinusitis. Harrison (1962) reported that 9 of 67 patients with vestibular neuronitis (defined according to Dix and Hallpike) had evidence of antral infection. Pfaltz (1955) reported sinusitis in 13 of 25 cases with vestibular neuronitis (defined according to Dix *and Hallpike).* Lumio and Aho (1965) reported sinusitis in of 40 patients with vestibular neuronitis.

In none of these studies was *the relative incidence of* sinusitis in patients with *multiple and* single attacks of dizziness compared. The present study shows a much higher incidence of sinusitis in patients with multiple attacks. Furthermore the follow up study indicates *that* the prognosis *of an isolated* vestibular deficit associated with sinusitis is poorer than the prognosis of

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Table 2. Tinnitus and fullness in "normal" and vestibular neuronitis groups

	Tinnitus				Fullness			
	Normal		Vestibular neuronitis		Normal		Vestibular neuronitis	
	No.	%	No.	%	No.		No.	%
Localized to one ear	34	11.4	8	17.4	24	11.4	3	6.5
Bilateral or nonlocalizable	72	24.2	13	28.2	37	12.5	6	13.0
None	191	64.3	25	54.3	236	87.5	37	80.4
Total	287		46		297		46	

vestibular neuronitis is compared with the incidence among 297 consecutively examined normal patients (with normal ENG's and normal audiograms). Slightly higher percentages of both bilateral and unilateral tinnitus occurred among the vestibular neuronitis patients. However this difference is not statistically significant (see Appendix, VI). There was also no significant difference in incidence of fullness between the normal and vestibular neuronitis groups.

Of the 8 vestibular neuronitis patients with unilateral tinnitus, 6 complained of tinnitus on the side of the vestibular deficit and 2 complained of tinnitus on the opposite side. This is suggestive, but would be expected to occur as a result of chance about 3 times out of 20, and therefore also cannot be considered significant.

Thus, although we have encountered suggestive complaints of tinnitus and fullness in patients with vestibular neuronitis, these cannot be shown to differ significantly from the complaints that would be expected from a group of patients not suffering from any identifiable auditory or vestibular disorder.

Rapidity of onset

The onset of vestibular neuronitis is frequently described as extremely rapid: a perfectly normal patient is "struck down" by a devastating attack of vertigo which renders him completely immobile. In our experience the onset of vestibular neuronitis, while more sudden than usually encountered in vestibular disorders, is not this rapid. The patients frequently complain of a prodromal period which may last from hours to days. During this period, there is a distinct feeling of "light-headedness" or being "off balance". In some instances, the prodrome may be sufficiently severe that the patient goes to bed. The typical onset of vestibular neuronitis is demonstrated by the three cases presented below.

Associated changes in taste

In 2 of the 46 patients, there were distinct changes in taste on the same side of the tongue as the side of the vestibular deficit. One patient noticed

SECTION II OTHER CHARACTERISTICS OF VESTIBULAR NEURONITIS

In this section we will discuss those characteristics of vestibular neuronitis which either are not unique to the entity and therefore should not be included in the definition or which require narrative description and therefore do not lend themselves to the type of statistical analysis used in Section I.

MATERIAL

A study of 46 patients with vestibular neuronitis, defined as proposed in the preceding section, is presented. Thirty were included in the population analyzed in Section I. An additional 16 patients were added from subsequent clinical material.

RESULTS

Sex incidence

Of the 46 patients with vestibular neuronitis, 20 were male and 26 were female. In a series of 45 patients with comparable clinical patterns, Lachman and Stahle (1967) reported that 27 were male and 18 were female. In a series of 40 vestibular neuronitis cases reported by Lumio and Aho (1965) (less comparable to ours since two patients had directional preponderance) 16 were male and 24 were female. In none of these series was one sex significantly (at the .05 level) predominant over the other. It is therefore concluded that vestibular neuronitis shows no significant preference for either sex.

Complaints of tinnitus and fullness

It has been reported that not only is hearing normal in vestibular neuronitis, but there is also a total absence of any complaint referable to the auditory system. We have been unable to confirm this. Although, by definition none of the 46 patients had a significant hearing loss several complained of tinnitus and/or fullness in either one or both ears, often associated with the onset of vertigo (cf. cases 1 and 2). However individuals with no identifiable auditory or vestibular pathology also often complain of tinnitus and fullness. Therefore before these complaints can be considered significant among patients with vestibular neuronitis, they must be compared with the incidence among "normal" patients.

In Table 2 the incidence of tinnitus and fullness in the 46 patients with

Table 2. *Tinnitus and fullness in "normal" and vestibular neuronitis groups*

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Associated changes in taste

In 2 of the 46 patients, there were distinct changes in taste on the same side of the tongue as the side of the vestibular deficit. One patient noticed

a loss of taste function on the involved side coincident with the onset of vertigo, and electrotaste testing confirmed reduced function The other patient (case 2) complained of a metallic taste on the involved side It thus appears that the (inflammatory?) process which presumably involves the vestibular nerve (see below) may also sometimes involve the chorda tympani

Galvanic responses

In their original description of vestibular neuronitis, Dix and Hallpike (1952) reported absent galvanic responses Since the galvanic stimulus supposedly acts at a point central to the end organ this was thought to indicate involvement of the vestibular nerve rather than the end organ therefore they proposed the term "vestibular neuronitis." To the knowledge of the author the absence of galvanic responses in vestibular neuronitis has not been independently confirmed

We have found that the body sway response to galvanic stimulation, which consists of sway toward the positive electrode (applied to the mastoid area) and away from the negative electrode occurs with much lower stimulus levels than the nystagmic response (Coats, 1968) Because of this lower threshold body sway responses to unilateral stimulation are always easily obtained In contrast the nystagmic response to unilateral stimulation can not be obtained because it requires painful current levels.

By recording the body sway response to galvanic stimulation a quantitative evaluation of unilateral galvanic responses can be obtained The amplitudes of the four galvanic responses (right− left− right+ left+) to monaauricular monopolar stimulation are measured and galvanic directional preponderance and unilateral weakness are computed as with the four caloric responses

Body sway galvanic tests in two patients with vestibular neuronitis have been obtained One is presented as case 3 In both patients, a galvanic unilateral weakness on the side of the caloric weakness was present Thus, our results support those of Dix and Hallpike and suggest that the lesion producing "vestibular neuronitis does, indeed involve the vestibular nerve

CASE REPORTS

The following three cases are representative of the entity vestibular neuronitis, defined as proposed in Section I

Case 1

This 41 year-old Caucasian housewife with a chief complaint of dizziness, had been in excellent health until one morning 20 days before the ENC examination when she felt vaguely dizzy and nauseated with no definite sensation of vertiginous spin She performed her normal morning activities, but in the afternoon she felt so ill that she went to bed and remained there for

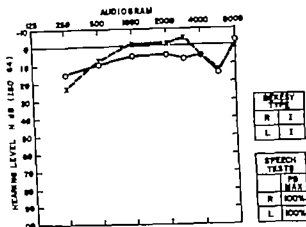


Fig. 10. Audiometric examination, Case 1

three days. During this time, she felt quite well as long as she lay quietly but the sensation of seasickness would return when she arose and she vomited once or twice when attempting this. After three days, she felt completely well, but five days later (12 days before the ENG) the difficulty returned, now with a definite sensation of spinning to her right. The severe vertigo persisted for three days, with several episodes of nausea and vomiting, then gradually subsided. At the time of the ENG examination, she complained only of a slightly off-balance sensation, but the vertigo would return with rapid head movement.

During her illness, the patient noted a roaring tinnitus "somewhere in my head." This could not be lateralized to either ear.

About a week before the initial episode of dizziness, the patient had had an unusually severe cold, consisting of a stuffy nose and sore throat. She did not notice fever. There was no history of ototoxic-drug intake.

Results of examination of her ears, nose and throat, and a complete neurological examination on the day before the ENG examination showed no nystagmus and were otherwise entirely normal except for a tendency to sway to either side in tandem stance. Roentgenograms of the skull were normal. Audiometric-examination results (Fig. 10) also were normal. The ENG examination showed a moderately intense left-beating spontaneous nystagmus (Fig. 11) and an almost complete absence of caloric responses from the right labyrinth (Fig. 12).

Three months after the ENG examination, the patient was followed up by telephone. She had experienced some residual unsteadiness for about a month after the examination, but since then had remained entirely symptom-free.

Comment. This is a typical example of vestibular neuronitis. The history well illustrates that the onset of the vertigo is usually not "sudden" or "precipitous" as it is sometimes described.

a loss of taste function on the involved side coincident with the onset of vertigo, and electrotaste testing confirmed reduced function The other patient (case 2) complained of a metallic taste on the involved side It thus appears that the (inflammatory*) process which presumably involves the vestibular nerve (see below) may also sometimes involve the chorda tympani

Galvanic responses

In their original description of vestibular neuronitis, Dix and Hallpike (1952) reported absent galvanic responses Since the galvanic stimulus supposedly acts at a point central to the end organ this was thought to indicate involvement of the vestibular nerve rather than the end organ therefore they proposed the term vestibular neuronitis. To the knowledge of the author the absence of galvanic responses in vestibular neuronitis has not been independently confirmed

We have found that the body sway response to galvanic stimulation which consists of sway toward the positive electrode (applied to the mastoid area) and away from the negative electrode occurs with much lower stimulus levels than the nystagmic response (Coats, 1968) Because of this lower threshold body sway responses to unilateral stimulation are always easily obtained In contrast the nystagmic response to unilateral stimulation cannot be obtained because it requires painful current levels.

By recording the body sway response to galvanic stimulation a quantitative evaluation of unilateral galvanic responses can be obtained The amplitudes of the four galvanic responses (right − left − right + left +) to monauricular monopolar stimulation are measured and galvanic directional preponderance and unilateral weakness are computed as with the four caloric responses.

Body sway galvanic tests in two patients with vestibular neuronitis have been obtained One is presented as case 3 In both patients a galvanic unilateral weakness on the side of the caloric weakness was present Thus, our results support those of Dix and Hallpike and suggest that *the lesion producing "vestibular neuronitis" does, indeed* involve the vestibular nerve

CASE REPORTS

The following three cases are representative of the entity vestibular neuronitis, defined as proposed in Section I

Case 1

This 41 year-old Caucasian housewife with a chief complaint of dizziness, had been in excellent health until one morning, 20 days before the ENC examination when she felt vaguely dizzy and nauseated with no definite sensation of vertiginous spin She performed her normal morning activities, but in the afternoon she felt so ill that she went to bed and remained there for

Case 2

This 35-year-old Latin American man was in generally excellent health until six days before the ENG examination, when he noted a light headed feeling while driving to work. This light headed feeling persisted throughout the morning and was accompanied by nausea. He went to bed in the afternoon and experienced some relief but the following morning, after arising, he experienced severe true vertigo, with nausea and vomiting, and entered the hospital. At this time the patient noted a distinct metallic taste on the left side of his tongue. He had a slight roaring in his head, but could not tell whether this was on the right or left side. He did not notice a loss of hearing. There was no history of a recent infection, and the patient had had no medications of any kind.

On admission, the patient appeared acutely ill and showed a second degree spontaneous nystagmus to the right. Ear, nose, and throat examinations revealed no abnormality. Neurological-examination results were negative except for the spontaneous nystagmus and a tendency to past point to the left. The spontaneous nystagmus subsided during the patient's hospital stay and, at the time of the ENG examination (four days after admission) it was barely perceptible on extreme right gaze. Tuning fork testing of the patient's hearing revealed no abnormality. Roentgenograms of the petromastoid portions of both temporal bones were normal.

The ENG examination of this patient is shown in Figs. 13 and 14. With eyes closed, an extremely intense right-beating nystagmus was present (Fig 13); hence the caloric responses (Fig. 14) which are superimposed on this intense nystagmus, show a marked directional preponderance to the right. In addition, the caloric test shows a marked unilateral weakness on the left.

The patient was discharged six days after admission. He was still ex

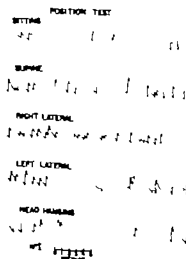


Fig. 13. Position test, Case 2.

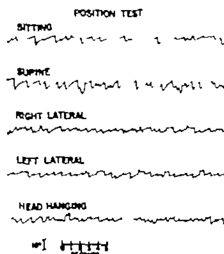
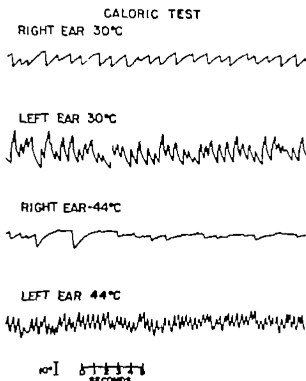


Fig 11 Po ition test, Case 1 In all ENG records presented, upward pen deflecti rej re sents eye deviation to the right.



	LATENCY OF NYS SEC	DURATION OF NYS SEC	ANALYSIS OF MAX. NYS		
			AMPL.	FREQ.	SPEED SLOW COMP.
30°C	[illegible]	[illegible]	[illegible]		[illegible]
30°C	[illegible]	[illegible]	[illegible]		[illegible]
44°C	[illegible]	[illegible]			[illegible]
44°C	[illegible]	[illegible]			[illegible]

Fig 12 Cal ri test Case 1

Case

This 35-year-old Latin American man was in generally excellent health until six days before the ENG examination, when he noted a light headed feeling while driving to work. This light headed feeling persisted through out the morning and was accompanied by nausea. He went to bed in the afternoon and experienced some relief but the following morning, after arising, he experienced severe, true vertigo, with nausea and vomiting, and entered the hospital. At this time the patient noted a distinct metallic taste on the left side of his tongue He had a slight roaring in his head, but could not tell whether this was on the right or left side. He did not notice a loss of hearing. There was no history of a recent infection, and the patient had had no medications of any kind.

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The ENG examination of this patient is shown in Figs. 13 and 14 With eyes closed, an extremely intense right-beating nystagmus was present (Fig 13) hence the caloric responses (Fig. 14) which are superimposed on this intense nystagmus, show a marked directional preponderance *to the right* In addition, the caloric test shows a marked unilateral weakness on the left.

The patient was discharged six days after admission He was still ex

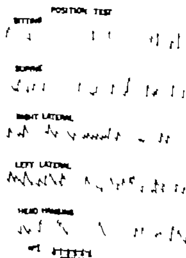


Fig 13 Position test, Case 2.

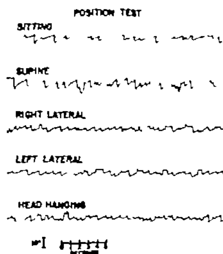


Fig 11 Position te t, Case 1 In all ENG record presented upward pen d flectl n represents eve deviation to the right

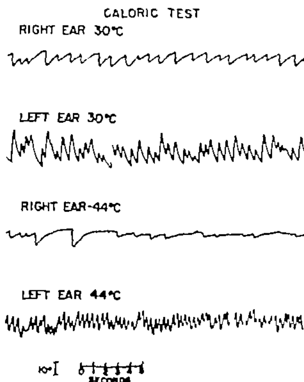


Fig 12 Calori t t *Case 1*

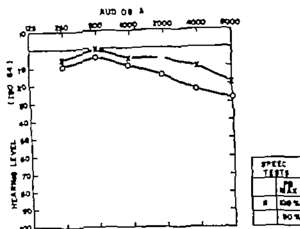


Fig 15 Audiogram, Case 3.

and vomiting He was admitted to the hosiptal that evening The patient gave a history of occasional bilateral, ringing tinnitus and mild hearing loss for about five years. There was no change in auditory function associated with his present illness, no antecedent infection, and no history of ototoxic-drug intake

CALORIC NYSTAGMUS

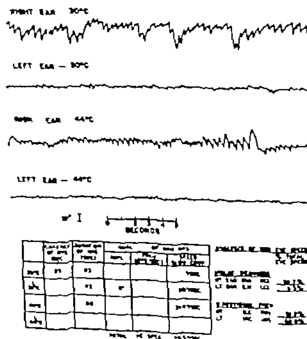
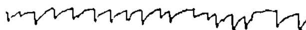


Fig 16 Caloric test, Case 3

CALORIC NYSTAGMUS

RIGHT EAR 31°C



LEFT EAR 31 C



RIGHT EAR 43 C



LEFT EAR 43 C



10° I 0 5 SECONDS

	[illegible]	[illegible]	[illegible]		
			[illegible]	[illegible]	[illegible]
[illegible]			[illegible]		[illegible]
[illegible]	[illegible]	[illegible]	[illegible]		[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	1	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]		[illegible]

Fig 11 Caloric test, Case 2

periencing some unsteadiness, but his vertigo had almost completely cleared One week later he was almost completely symptom free but was still experiencing residual unsteadiness which was aggravated by rapid head movement The patient was tested one month prior to writing this report and, therefore long term follow up is not available

Comment This patient also illustrates the typical picture of vestibular neuronitis, including the relatively gradual onset of vertigo The case is included because of the history of involvement of taste function on the same side as the vestibular deficit Also of interest is the nonlateralizable roaring tinnitus

Case 3

Five days before the ENG examination this 62 year-old Caucasian man noted a brief mild episode of dizziness which subsequently cleared spontaneously On the next day he awoke feeling "a little drunk" and by noon he was experiencing severe rotatory vertigo from left to right with nausea

days. (4) Two patients showed evidence of impaired taste function on the side of the vestibular deficit, thus suggesting involvement of the chorda tympani. (5) On two patients, body sway galvanic tests were obtained. Both showed galvanic deficits on the side of the vestibular deficit thus supporting a neural location of the lesion.

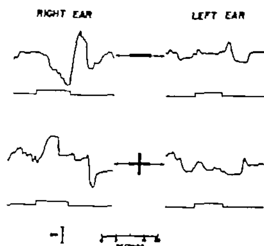


Fig 17 Body sway galvanic test, Case 3 Upward pen deflection represents sway to the right

On admission the patient appeared acutely ill and showed a third-degree spontaneous nystagmus to the right Ear nose throat and neurological examinations were essentially normal except for the spontaneous nystagmus. Roentgenograms of the mastoid portions of the temporal bones were within normal limits An audiometric examination (Fig 15) showed a mild high frequency loss in both ears, somewhat more pronounced on the right The spontaneous nystagmus progressively subsided and both it and the vertigo were gone 72 hours after admission

The ENG examination was done five days after admission A right beating spontaneous nystagmus of low to moderate intensity was present It tended to wax and wane throughout the position test so the effect of position could not be reliably assessed The caloric test showed a severe unilateral weakness on the left (Fig 16)

A body sway galvanic test was done on this patient The results are shown in Fig 17 There was a significant galvanic unilateral weakness on the left

Comment This patient is somewhat older than the usual patient with vestibular neuronitis, but this illustrates that the age incidence is not strictly limited The galvanic unilateral weakness on the same side as the caloric weakness supports the neural location of the vestibular lesion in vestibular neuronitis

SUMMARY OF SECTION II

A series of 46 patients with vestibular neuronitis, according to the definition proposed in Section I was studied It was found that (1) There was no sex predominance (2) Some patients complained of tinnitus and fullness, but the incidence of such complaints did not differ significantly from that found in a group of patients with normal auditory and vestibular function (3) The onset of vertigo typically occurred over a period of hours or even

days. (4) Two patients showed evidence of impaired taste function on the side of the vestibular deficit, thus suggesting involvement of the chorda tympani. (5) On two patients, body sway galvanic tests were obtained. Both showed galvanic deficits on the side of the vestibular deficit, thus supporting a neural location of the lesion.

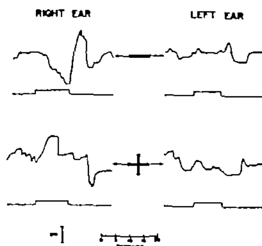


Fig 17 Body sway galvanic test, Case 3 Upward pen deflection represents sway to the right

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Comment This patient is somewhat older than the usual patient with vestibular neuronitis, but this illustrates that the age incidence is not strictly limited The galvanic unilateral weakness on the same side as the caloric weakness supports the neural location of the vestibular lesion in vestibular neuronitis

SUMMARY OF SECTION II

A series of 40 patients with vestibular neuronitis, according to the definition proposed in Section I was studied It was found that (1) There was no sex predominance (2) Some patients complained of tinnitus and fullness, but the incidence of such complaints did not differ significantly from that found in a group of patients with normal auditory and vestibular function (3) The onset of vertigo typically occurred over a period of hours or even

APPENDIX

STATISTICAL TESTS

The statistical procedures used to obtain the measurements of significance (P values) referred to in the text are outlined below. P values between .05 and .001 are referred to as "significant" in the text. P values of less than .001 are referred to as "highly significant". Because patients' ages and amounts of unilateral weakness and spontaneous nystagmus were not normally distributed, nonparametric tests were used. All P values are two-tail.

I. *Incidence of multiple and single attacks*

A. *Test*: Chi square

B. *Results*

1. Significance of differences among 3 groups (A & N, N-only, Normal)
   $\chi^2 = 66.410$ degrees of freedom: 3 $P < .001$
2. A & N (110 patients) versus Normal (418 patients)
   $\chi^2 = 12.80$ degrees of freedom: 1 $P < .001$
3. N-only (76 patients) versus Normal
   $\chi^2 = 75.543$ degrees of freedom: 1 $P < .001$
4. N-only versus A & N
   $\chi^2 = 12.82$ degrees of freedom: 1 $P < .001$

C. *Conclusion*

Significant differences in incidence of multiple versus single attacks exist between all 3 groups.

II. *Patients' ages*

A. *Tests*: Kruskal-Wallace one-way analysis of variance for differences among all subgroups. Mann-Whitney U test for differences between individual groups and subgroups. Correction for ties was not employed.

B. *Results*

1. Significance of differences among 6 subgroups
   $H = 12.8$ degrees of freedom: 5 $P = .023$
2. A & N and Normal multiple (482 patients) versus A & N and Normal, single (46 patients)
   $Z = 0.736$
   $P < .237 > .230$
3. A & N and Normal (528 patients) versus N-only multiple (47 patients)
   $Z = 0.793$
   $P < .215 > .212$

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APPENDIX

STATISTICAL TESTS

The statistical procedures used to obtain the measurements of significance (P values) referred to in the text are outlined below P values between 05 and 001 are referred to as "significant In the text. P values of less than 001 are referred to as highly significant" Because patients ages and amounts of unilateral weakness and spontaneous nystagmus were not normally distributed, nonparametric tests were used All P values are two-tail

I *Incidence of multiple and single attacks*

A. *Test* Chi square

B *Results*

1 Significance of differences among 3 groups (A & V V-only Normal)

$\chi^2 = 66\ 410$ degrees of freedom. 3 $P < 001$

2 A & V (110 patients) versus Normal (418 patients)

$\chi^2 = 12.80$ degrees of freedom. 1 $P < 001$

3 V-only (76 patients) versus Normal

$\chi^2 = 75.543$ degrees of freedom. 1 $P < 001$

4 V-only versus A & V

$\chi^2 = 12.82$ degrees of freedom. 1 $P < 001$

C *Conclusion*

Significant differences in incidence of multiple versus single attacks exist between all 3 groups

II *Patients ages*

A *Tests* Kruskal Wallace one-way analysis of variance for differences among all subgroups. Mann-Whitney U test for differences between individual groups and subgroups. Correction for ties was not employed.

B *Results*

1 Significance of differences among 6 subgroups

$H = 12.8$ degrees of freedom. 5 $P \sim 025$

2 A & V and Normal, multiple (482 patients) versus A & V and Normal, single (46 patients)

$Z = 0\ 730$

$P < 237 > 230$

3 A & V and Normal (528 patients) versus V-only multiple (47 patients)

$Z = 0\ 93$

$P < 215 > 212$

4 A & V and Normal (528 patients) versus V-only single (20 patients)
   $Z = 2\ 962$ $P \approx 003$
5 V only single versus V-only multiple
   $Z = 2\ 273$ $P \approx 02$

C *Conclusion*
The difference in median ages among all subgroups is almost completely accounted for by the tendency for patients in the V-only single-attack subgroup to be younger than patients in the other subgroups

III *Incidence and type of infection*

A *Test* Chi square

B *Results*

1 Significance of differences in incidence among 3 groups
   $\chi^2 = 42\ 063$ degrees of freedom 2 $P < 001$
2 A & V versus Normal
   $\chi^2 = 5\ 559$ degrees of freedom 1 $P < 02 > 01$
3 V-only versus A & V
   $\chi^2 = 9\ 243$ degrees of freedom 1 $P < 005 > 001$
4 V only versus Normal
   $\chi^2 = 41\ 230$ degrees of freedom 1 $P < 001$
5 Incidence of sinusitis in V only multiple group versus incidence in all other patients
   $\chi^2 = 28\ 149$ degrees of freedom 1 $P < 001$

C *Conclusion*
All groups differ significantly in incidence of infection The incidence of *sinusitis in the V only multiple subgroup is significantly higher* than among all other patients

IV *Incidence intensity and direction of spontaneous nystagmus*

A *Test* Chi square Spontaneous nystagmus classified as follows (1) no spontaneous nystagmus (2) spontaneous nystagmus toward UW (3) *spontaneous nystagmus away from UW low intensity* (4) spontaneous nystagmus away from UW moderate and high intensity

B *Results*

1 Significance of difference between 2 groups
   $\chi^2 = 5\ 13$ *degrees of freedom 1* $P < 025 > 020$
2 Significance of differences among 4 subgroups
   $\chi^2 = 56\ 248$ degrees of freedom 9 $P < 001$
3 A & V single versus V-only multiple
   $\chi^2 = 6\ 684$ *degrees of freedom 3* P 10 05
4 A & V single versus A & V multiple
   $\chi^2 = 7\ 550$ degrees of freedom 3 $P < 10 > 05$

5. A & V multiple versus V-only single
   $\chi^2 = 1.998$ degrees of freedom 3 $P < .70 > .50$
6. V-only single versus V-only multiple
   $\chi^2 = 32.187$ degrees of freedom 3 $P < .001$
7. V-only single versus A & V multiple
   $\chi^2 = 40.800$ degrees of freedom 3 $P < .001$
8. V-only-single versus A & V single
   $\chi^2 = 8.187$ degrees of freedom 3 $P < .05 > .025$

C. *Conclusion*

The difference in spontaneous nystagmus among the subgroups is completely accounted for by the strong tendency for spontaneous nystagmus in the V-only-single-attack subgroup to be relatively intense and directed away from the side of the unilateral weakness.

V. *Amount of unilateral weakness*

A. *Tests*: Kruskal-Wallace test for differences among all groups. Mann-Whitney U test for differences between individual subgroups. Correction for ties not employed.

B. *Results*

1. Significance of differences among 4 subgroups
   $H = 23.971$ degrees of freedom 3 $P < .001$
2. A & V multiple (91 patients) versus A & V-single (19 patients)
   $Z = 1.050$ $P \approx .294$
3. A & V-single versus V-only-single (29 patients)
   $Z = 0.770$ $P \approx .450$
4. A & V multiple (91 patients) versus V-only-single
   $Z = 2.020$ $P \approx .043$
5. V-only multiple (47 patients) versus V-only-single
   $Z = 4.218$ $P < .001$
6. V-only multiple versus A & V multiple
   $Z = 3.623$ $P < .001$
7. V-only multiple versus A & V-single
   $Z = 2.886$ $P \approx .004$

C. Conclusion

The significant difference in amount of unilateral weakness between all subgroups is completely accounted for by the low median unilateral weakness in the V-only multiple-attack subgroup. The difference between the A & V multiple-attack and V-only-single-attack subgroups is of questionable significance because the A & V multiple and A & V-single subgroups do not differ significantly and the A & V-single and V-only-single also do not differ significantly.

VI *Incidence of tinnitus*

A *Test* Chi square The significance of the differences in incidence of tinnitus between normal (297 patients) and vestibular neuronitis (46 patients) groups was tested Also a test was made for significant differences in relative incidence of lateralizable tinnitus non lateralizable tinnitus and no tinnitus in the normal and vestibular neuronitis groups

B *Results*

1 Significance of difference between incidence of tinnitus

$\chi^2 = 1\ 70$ degrees of freedom 1 $P \approx 0\ 20$

2 Significance of differences between incidences of lateralizable nonlateralizable and no tinnitus

$\chi^2 = 2\ 03$ degrees of freedom 2 $P <$ 50 > 30

C Conclusion

The incidence of tinnitus in the normal group does not differ significantly from the incidence in the vestibular neuronitis group Since there are even smaller differences in incidence of fullness, these differences must also be insignificant